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FILE LAST UPDATED: 25 Feb 2003 (20030225/ED)

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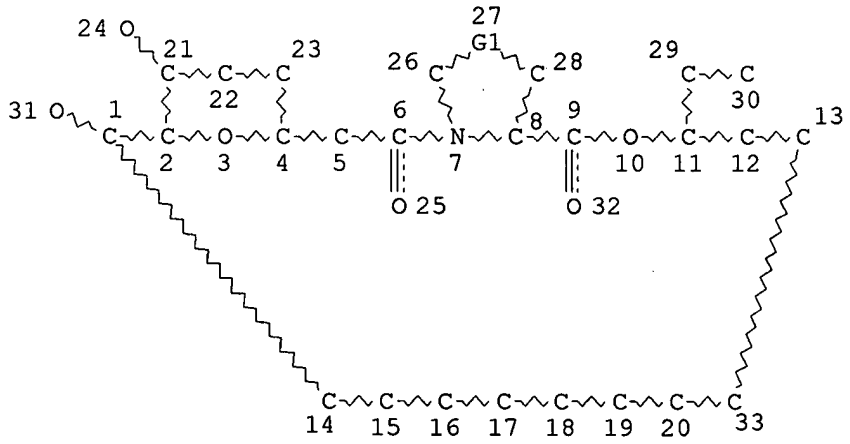

REP G1=(0-5) C
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
MLEVEL IS CLASS AT 21 22 23
DEFAULT ECLEVEL IS LIMITED
ECOUNT IS UNLIMITED AT 21 22 23

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 33

STEREO ATTRIBUTES: NONE
L9 3512 SEA FILE=REGISTRY SSS FUL L7
L10 3995 SEA FILE=HCAPLUS L9
L12 27 SEA FILE=HCAPLUS L10 (L) (EYE? OR OPHTHAL? OR OCUL?)

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L12 ANSWER 1 OF 27 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:77534 HCAPLUS
TITLE: Compositions and methods for enhancing drug delivery across and into ocular tissues
INVENTOR(S): Rothbard, Jonathan B.; Wender, Paul A.; McGrane, P. Leo; Sista, Lalitha V. S.; Kirschberg, Thorsten A.
PATENT ASSIGNEE(S): Cellgate, Inc., A Delaware Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 64 pp., Cont.-in-part of U.S. Ser. No. 792,480.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003022831	A1	20030130	US 2002-83960	20020225
US 2002127198	A1	20020912	US 2001-792480	20010223

PRIORITY APPLN. INFO.: US 1999-150510P P 19990824
US 2000-648400 A2 20000824
US 2001-792480 A2 20010223

AB This invention provides compns. and methods for enhancing delivery of drugs and other agents across epithelial tissues, including into and across ocular tissues and the like. The compns. and methods are also useful for delivery across endothelial tissues, including the blood brain barrier. The compns. and methods employ a delivery-enhancing transporter that has sufficient guanidino or amidino side chain moieties to enhance delivery of a compd. conjugated to the reagent across one or more layers of the tissue, compared to the non-conjugated compd. The delivery-enhancing polymers include, for example, polyarginine mols. that are preferably between about 6 and 25 residues in length.

IT **104987-11-3**, FK506
RL: RCT (Reactant); RACT (Reactant or reagent)
(delivery-enhancing transporters for drug delivery across and into **ocular** tissues)

IT **491875-85-5P 491875-86-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(delivery-enhancing transporters for drug delivery across and into **ocular** tissues)

IT **491875-78-6P 491875-79-7P 491875-80-0P 491875-81-1P 491875-82-2P 491875-83-3P 491875-84-4P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(delivery-enhancing transporters for drug delivery across and into **ocular** tissues)

L12 ANSWER 2 OF 27 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:58810 HCAPLUS
DOCUMENT NUMBER: 138:83428
TITLE: Tacrolimus formulations for the treatment of ocular disease
INVENTOR(S): Peyman, Gholam A.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 6 pp., Cont.-in-part of U.S. Pat. Appl. 2002 13,340.

CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003018044	A1	20030123	US 2002-247220	20020919
US 2002013340	A1	20020131	US 2000-507076	20000218
US 6489335	B2	20021203		

PRIORITY APPLN. INFO.: US 2000-507076 A2 20000218

AB A formulation to treat ocular disease,e.g. dry eye disease, as well as other diseases, is disclosed. Tacrolimus is administered intraocularly, e.g. topically or by injection. For topical administration, an amt. of about 1 ng to 10 .mu.g may be formulated in an aq. based cream that may be applied at bedtime or throughout the day. For injection, a dose of about 20-1000 .mu.g/mL is used. Tacrolimus may also be administered in milligram quantities as a surgical implant contained in a diffusible walled reservoir sutured to the wall of the sclera, or may be contained within an inert carrier such as microspheres or liposomes to provide a slow-release drug delivery system.

IT **104987-11-3**, Tacrolimus
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tacrolimus formulations for treatment of **ocular** disease)

L12 ANSWER 3 OF 27 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:909458 HCAPLUS
DOCUMENT NUMBER: 138:11234
TITLE: Studies on the effects of the immunosuppressant FK-506 on the high-risk corneal graft rejection
AUTHOR(S): Wang, Minhua; Lin, Yuesheng; Chen, Jiaqi; Liu, Yongming; Xie, Hanping; Ye, Chengtian
CORPORATE SOURCE: Zhongshan Ophthalmic Center, Sun Yat-sen University, Canton, 510060, Peop. Rep. China
SOURCE: Eye Science (2002), 18(3), 160-164
CODEN: YAXUE3; ISSN: 1000-4432
PUBLISHER: Zhongshan Ophthalmic Center
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To evaluate the clin. efficacy of FK-506 on suppressing high-risk cornea transplantation rejection. In a randomized controlled clin. trial, 56 eyes of 56 patients with high-risk keratoplasty (including total corneal transplantation TCT, total corneal transplantation with circular lamellar sclera CST, vascularization corneal transplantation and corneal retransplantation) were divided into the exptl. group and the control group (each with 28 eyes). The exptl. group was treated by FK-506 eyedrops (0.5 mg/mL) and TobraDex eyedrops, compared with the control group that was treated by 1% CsA eyedrops and TobraDex eyedrops. In the av. 8.1-mo follow-up period, the visual acuity, graft transparent duration and Rejection Index (RI) of grafts were obsd. In the follow-up period, the graft rejection rate of the exptl. and the control group was 63.6% and 95.2% resp. ($X2 = 4.72$, $P<0.05$) with significant difference. The local application of FK-506 suppressed effectively the graft rejection of corneal transplantation of the patients at high risk.

IT **104987-11-3**, FK-506
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of immunosuppressant FK-506 and TobraDex **eyedrops** vs. CsA (Sandimmune) and TobraDex **eyedrops** on high-risk

corneal graft rejection in humans)
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 27 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:832614 HCAPLUS
DOCUMENT NUMBER: 137:329460
TITLE: Macrocyclic agent for topical ophthalmic treatment of ocular inflammatory diseases
INVENTOR(S): Ueno, Ryuji
PATENT ASSIGNEE(S): Sucampo A.-G., Switz.
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002085359	A1	20021031	WO 2002-JP3664	20020412
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002187998	A1	20021212	US 2002-120515	20020412

PRIORITY APPLN. INFO.: US 2001-283169P P 20010412
OTHER SOURCE(S): MARPAT 137:329460
AB The present invention provides an agent for topical ophthalmic treatment of a human for ocular inflammatory diseases, contg. a tricyclo compd. such as FK506 as the active ingredient in the concn. of 0.01% - 0.1%. The present agent for topical ophthalmic treatment continuously shows superior ocular anti-inflammatory effects by topically administering it in a low dose to the eye of the human having the ocular inflammatory diseases. The present agent is effective for symptoms caused by the ocular inflammatory diseases such as itching, flare, edema, ulcer, etc. The present agent is also effective for a subject in whom conventional anti-inflammatory agents show no improving effect (e.g., steroid and cyclosporins). The present agent is also effective for a subject for whom other anti-inflammatory agents cannot be used (e.g., steroid contraindication). Decreases in itching in patients were greated in exptl. groups instilled with 0.01, 0.06, and 0.1% FK506 eyedrops than in the control groups instilled with placebo.
IT **104987-11-3**, Fk506
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(macrocyclic agent for topical **ophthalmic** treatment of **ocular** inflammatory diseases)
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 5 OF 27 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:428756 HCAPLUS
DOCUMENT NUMBER: 137:10999
TITLE: Methods for reducing or preventing transplant rejection in the eye and intraocular implants for use

therefor
INVENTOR(S): Wong, Vernon G.
PATENT ASSIGNEE(S): Oculex Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002043785	A2	20020606	WO 2001-US44481	20011128
WO 2002043785	A3	20021121		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002036495	A5	20020611	AU 2002-36495	20011128
US 2002182185	A1	20021205	US 2001-997094	20011128

PRIORITY APPLN. INFO.: US 2000-250023P P 20001129
US 2001-298253P P 20010612
WO 2001-US44481 W 20011128

AB Methods for reducing or preventing transplant rejection in the eye of an individual are described, comprising: (a) performing an ocular transplant procedure; and (b) implanting in the eye a bioerodible drug delivery system comprising an immunosuppressive agent and a bioerodible polymer. Sustained-release intraocular implant contg. HPMC 15, PLGA 35, and dexamethasone 50% were prepd. The implants were implanted in the anterior chamber of the rat eyes at the end of cornea transplants surgery. Rats did not show any sign of rejection and the corneas stayed clear in all eyes. After 8 wk the graft survival was 100%.

IT **104987-11-3**, Tacrolimus
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for reducing or preventing transplant rejection in **eye** and intraocular implants for use therefor)

L12 ANSWER 6 OF 27 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:113132 HCAPLUS
DOCUMENT NUMBER: 136:156478
TITLE: Topical compositions containing tacrolimus for treatment of immunological disease at front and surface of eyes
INVENTOR(S): Chen, Jia-qi; Liu, Yong-min
PATENT ASSIGNEE(S): Zhongshan University of Medical Science, Zhongshan Ophthalmology Center, Peop. Rep. China
SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

JP 2002047186	A2	20020212	JP 2001-82456	20010322
CN 1333018	A	20020130	CN 2000-117235	20000707
US 2002173516	A1	20021121	US 2001-888342	20010622

PRIORITY APPLN. INFO.: CN 2000-117235 A 20000707

AB The invention relates to a topical compns. contg. tacrolimus hydrate or tacrolimus anhydride as an active ingredient for treatment of immunol. disease at front and surface of eyes, esp. in a form of an eye drop or an ophthalmic paste. An eye drop compn. contg. tacrolimus (FK506) 0.05, polyethylene hydrogenated castor oil 1, thickener 0.3, NaCl 0.75, antibacterial agent 0.002, and water q.s. to 100 % was formulated.

IT **104987-11-3**, Tacrolimus **109581-93-3**, Tacrolimus hydrate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(topical compns. contg. tacrolimus for treatment of immunol. disease at front and surface of **eyes**)

L12 ANSWER 7 OF 27 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:90619 HCAPLUS
DOCUMENT NUMBER: 136:112708
TITLE: Tacrolimus formulation for the treatment of ocular diseases
INVENTOR(S): Peyman, Gholam A.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 4 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002013340	A1	20020131	US 2000-507076	20000218
US 6489335	B2	20021203		
US 2003018044	A1	20030123	US 2002-247220	20020919

PRIORITY APPLN. INFO.: US 2000-507076 A2 20000218

AB A formulation to treat ocular diseases, e.g. dry eye disease, as well as other diseases, is disclosed. Tacrolimus is administered either topically or by injection. For topical administration, an amt. of about 1 ng to 10 .mu./g may be formulated in an aq. based cream that may be applied at bedtime or throughout the day. For injection, a dose of about 20-1000 .mu.g/mL is used. Tacrolimus may also be administered in milligram quantities as a surgical implant contained in a diffusible walled reservoir sutured to the wall of the sclera, or may be contained within an inert carrier such as microspheres or liposomes to provide a slow-release drug delivery system.

IT **104987-11-3**, Tacrolimus
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tacrolimus formulation for treatment of **ocular** disease)

L12 ANSWER 8 OF 27 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:667846 HCAPLUS
DOCUMENT NUMBER: 136:339
TITLE: Treatment of ocular cicatricial pemphigoid with tacrolimus (FK 506)
AUTHOR(S): Letko, Erik; Ahmed, A. Razzaque; Foster, C. Stephen
CORPORATE SOURCE: Immunology and Uveitis Service, Boston, MA, 02116, USA
SOURCE: Graefe's Archive for Clinical and Experimental Ophthalmology (2001), 239(6), 441-444
CODEN: GACODL; ISSN: 0721-832X
PUBLISHER: Springer-Verlag

DOCUMENT TYPE: Journal
LANGUAGE: English

AB Purpose: To evaluate the efficacy of tacrolimus (FK 506) therapy in patients with ocular cicatricial pemphigoid (OCP). Methods: In a cohort study, six patients with OCP, in whom the disease was not controlled by conventional immunosuppressive agents administered in high doses for an appropriate period of time, were treated with FK 506. The FK 506 was administered orally at the daily dose of 8 mg. Final clin. response to FK 506 was divided into three categories based on the difference between severity of conjunctival inflammation before and after FK 506 therapy. "Total control" of disease activity was defined as residual inflammatory activity of 0.5 or less in the final examn. and an inflammation decrement of at least 0.5 between initial and final examn. "Partial control" was defined as final disease activity 1.0 or 1.5 and at least 0.5 decrement of disease activity between initial and final examn. "Uncontrolled inflammation" was defined as final disease activity above 1.5 or no improvement between initial and final activity. Results: The av. age of the patients was 67.5 yr (range 50-75 yr). Male to female ratio was 1:1. The av. duration of OCP prior to beginning of FK 506 treatment was 6.25 yr (range 3-12.5 yr). The av. duration of treatment with FK 506 was 11 mo (range 5-18 mo). The av. disease activity prior to the administration of FK 506 was 2.6 (range 2.0-3.0). The av. disease activity at the time when FK 506 was stopped was 2.0 (range 1.0-2.5). In four patients (67%) FK 506 failed to control activity of OCP, and in two patients (33%) the activity was controlled partially. Conclusions: Although FK 506 was not used in a prospective randomized trial and although the authors used the drug only in patients with OCP refractory to conventional immunosuppressive agents, it is likely that FK 506 is incapable of controlling the activity of OCP and inducing a remission.

IT **104987-11-3**, FK 506
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tacrolimus is ineffective in treatment of **ocular** cicatricial pemphigoid in humans)

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 9 OF 27 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:319758 HCAPLUS
DOCUMENT NUMBER: 134:331600
TITLE: Use of a CD40:CD154 binding interruptor to treat immunological complications of the eye
INVENTOR(S): Dana, M. Reza; Vaishnaw, Akshay K.; Burkly, Linda C.; Lobb, Roy; Adelman, Burt
PATENT ASSIGNEE(S): Biogen, Inc., USA; Schepens Eye Research Institute
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001030386	A1	20010503	WO 2000-US28945	20001019

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,

YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 1223981 A1 20020724 EP 2000-973678 20001019
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL
US 2003027744 A1 20030206 US 2002-125264 20020418
PRIORITY APPLN. INFO.: US 1999-160909P P 19991022
US 2000-196453P P 20000411
US 2000-229491P P 20000831
WO 2000-US28945 W 20001019

AB The invention relates generally to the treatment and inhibition of immunol. complications of the eye. Such complications include unwanted immune responses resulting in an ocular inflammatory disease, resulting from a corneal or retinal graft transplantation or resulting from ocular angiogenesis, particularly ocular neovascularization. The invention relates in particular to the inhibition, treatment, or reversal of immune-system driven rejection of grafted corneal or retinal tissue or cells in a recipient host and to the treatment or inhibition of ocular inflammatory disease or ocular neovascularization in a host. Compns. and methods disclosed herein capitalize on the discovery that immunol. complications of the eye can be inhibited using a CD40:CD154 binding interruptor, either alone or in combination with another immunomodulator or immunosuppressor. An exemplary CD40:CD154 binding interruptor is an anti-CD154 monoclonal antibody, such as an antibody having the antigen-specific binding characteristics of the 5c8 monoclonal antibody.

IT **104987-11-3**, Tacrolimus
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(use of a CD40:CD154 binding interruptor to treat immunol. complications of the **eye**)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 10 OF 27 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:319703 HCAPLUS
DOCUMENT NUMBER: 134:316155
TITLE: Controlled-release biocompatible ocular drug delivery implant devices and methods
INVENTOR(S): Wong, Vernon G.; Hu, Mae W. L.; Berger, Donald E., Jr.
PATENT ASSIGNEE(S): Oculex Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001030323	A2	20010503	WO 2000-US29004	20001019
WO 2001030323	A3	20020221		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6331313	B1	20011218	US 1999-426141		19991022
EP 1143935	A2	20011017	EP 2000-973704		20001019
EP 1143935	A3	20020918			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, IE, SI, LT, LV, FI, RO					
BR 2000007454	A	20011030	BR 2000-7454		20001019
NO 2001003094	A	20010822	NO 2001-3094		20010621
PRIORITY APPLN. INFO.:			US 1999-426141	A2	19991022
			WO 2000-US29004	W	20001019

AB Controlled-release devices are disclosed which are biocompatible and can be implanted into the eye. The devices have a core comprising a drug and a polymeric outer layer which is substantially impermeable to the entrance of an environmental fluid and substantially impermeable to the release of the drug during a delivery period, and drug release is affected through an orifice in the outer layer. These devices have an orifice area of less than 10 of the total surface area of the device and can be used to deliver a variety of drugs with varying degrees of soly. and or mol. wt. Methods are also provided for using these drug delivery devices. A teflon tube of 0.97 mm internal diam. and 1.31 mm outer diam. was used to prep. a cylindrical device with 5.7 mm long and comprising 3.3 mg of gentamicin.

IT **104987-11-3**, Tacrolimus
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled-release biocompatible **ocular** drug delivery implant devices having impermeable polymeric outer layers and drug core)

L12 ANSWER 11 OF 27 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:790310 HCAPLUS
DOCUMENT NUMBER: 133:317582
TITLE: Use of macrolide compounds for the treatment of dry eye
INVENTOR(S): Ueno, Ryuji
PATENT ASSIGNEE(S): R-Tech Ueno, Ltd., Japan
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2000066122	A1	20001109	WO 2000-JP2756		20000426
W: AL, AU, BR, CA, CN, CZ, HU, IL, IN, JP, KR, LT, LV, MK, MX, NO, NZ, RO, RU, SI, TR, US, ZA					
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
EP 1173177	A1	20020123	EP 2000-921047		20000426
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
BR 2000011225	A	20020319	BR 2000-11225		20000426
JP 2002543132	T2	20021217	JP 2000-615007		20000426
NO 2001005288	A	20011029	NO 2001-5288		20011029
PRIORITY APPLN. INFO.:			US 1999-132009P	P	19990430
			WO 2000-JP2756	W	20000426

OTHER SOURCE(S): MARPAT 133:317582

AB The present invention provides an agent for treating a dry eye, which contains a macrolide compd. such as FK506.

IT **104987-11-3**, FK506

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of macrolide compds. such as FK506 for treatment of dry **eye**)

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 12 OF 27 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:451211 HCAPLUS
DOCUMENT NUMBER: 131:92517
TITLE: Topical ophthalmic preparations containing immunosuppressive agents
INVENTOR(S): Stuchlik, Milan; Jegorov, Alexandr; Matha, Vladimir; Stuchlik, Josef
PATENT ASSIGNEE(S): Galena, A.S., Czech Rep.
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9934830	A1	19990715	WO 1998-CZ54	19981217
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CZ 287497	B6	20001213	CZ 1997-4237	19971230
CA 2317010	AA	19990715	CA 1998-2317010	19981217
AU 9914813	A1	19990726	AU 1999-14813	19981217
EP 1058560	A1	20001213	EP 1998-958793	19981217
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, FI, RO				
JP 2002500200	T2	20020108	JP 2000-527277	19981217
NO 2000003344	A	20000627	NO 2000-3344	20000627

PRIORITY APPLN. INFO.: CZ 1997-4237 A 19971230
WO 1998-CZ54 W 19981217

AB Disclosed are therapeutic prepns. for topical ophthalmic application, contg. 0.02-5.0 % of immunosuppressive agents belonging to the groups of monocyclic undecapeptides, macrolide lactones or corticosteroids, in a vehicle comprising up to 10 % of polyalkylene glycol-polyurethane copolymers. Said copolymers consist preferably of poly(oxy-1,2-ethanediyl)-.alpha.-hydro-.omega.-hydroxypolymers with 1,1'-methylene-bis-(4-isocyanatocyclohexane) having an av. mol. wt. of from 1000 to 3000 in a hydrophilic vehicle and preferably of poly[oxy(methyl-1,2-ethanediyl)]-.alpha.-hydro-.omega.-hydroxypolymers with 1,1'-methylene-bis-(4-isocyanatocyclohexane) having an av. mol. wt. of from 1600 to 18000 in a lipophilic vehicle. Said therapeutic agents can further contain addnl. excipients common in topical administration forms. An eye drop soln. contained ciclosporin 1, 4,4'-dicyclohexylmethane diisocyanate-polyethylene glycol copolymer 1, diglyceryl monooleate 2.5, chlorobutanol 0.5 kg, and maize oil to 100 L.

IT **104987-11-3**, Tacrolimus
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(topical **ophthalmic** prepns. contg. immunosuppressive agents)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 13 OF 27 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:432478 HCAPLUS
DOCUMENT NUMBER: 131:110793
TITLE: New topical treatments for ocular inflammatory disease. Cyclosporin, FK506 and NSAIDs
AUTHOR(S): Hikita, Naofumi
CORPORATE SOURCE: Sch. Med., Kurume Univ., Kurume, 830-0011, Japan
SOURCE: Atarashii Ganka (1999), 16(6), 775-780
CODEN: ATGAEX; ISSN: 0910-1810
PUBLISHER: Medikaru Ai Shuppan
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review with 18 refs., on action mechanism and ophthalmic application of eye drops contg. immunosuppressants including cyclosporin, FK506, and FTY720, and eye drops contg. nonsteroidal antiinflammatory drugs.
IT **104987-11-3**, FK506
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(topical treatment of **ocular** inflammatory diseases by cyclosporin, FK506, and NSAIDs)

L12 ANSWER 14 OF 27 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:521822 HCAPLUS
DOCUMENT NUMBER: 129:285735
TITLE: Cytokine production by T cells infiltrating in the eye of uveitis patients
AUTHOR(S): Sakaguchi, Mami; Sugita, Sunao; Sagawa, Kimitaka; Itoh, Kyogo; Mochizuki, Manabu
CORPORATE SOURCE: Departments of Ophthalmology, Kurume University School of Medicine, Kurume, Japan
SOURCE: Japanese Journal of Ophthalmology (1998), 42(4), 262-268
CODEN: JJOPA7; ISSN: 0021-5155
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The capacity of T cells to produce cytokines was investigated using T-cell clones (TCCs) established from infiltrating cells in the aq. humor (AH) or peripheral blood mononuclear cells (PBMC) of patients with Vogt-Koyanagi-Harada (VKH) disease or sarcoidosis. The cytokines produced and tested in the study were interleukin (IL)-1.alpha., IL-6, IL-8, interferon (IFN)-.gamma., tumor necrosis factor (TNF)-.alpha., and granulocyte monocyte colony stimulating factor (GM-CSF). All TCCs (n = 9) from AH of VKH patients spontaneously produced significantly larger amts. of IL-6, IL-8, and IFN-.gamma. than TCCs from healthy donor PBMC. All TCCs (n = 9) from AH of the sarcoidosis patient spontaneously produced significantly larger amts. of IL-1.alpha., IL-6, and IL-8 than TCCs from healthy donor PBMC. In addn., the effects of antiinflammatory drugs on the cytokine prodn. by the TCCs were investigated. Hydrocortisone significantly suppressed the prodn. of IL-6, IL-8, and GM-CSF by TCCs from AH of VKH patients. Tacrolimus also significantly suppressed the prodn. of IL-8 and GM-CSF by the TCCs. FTY720, an exptl. drug, suppressed only GM-CSF prodn. by TCCs from AH of VKH patients. Diclofenac failed to suppress the prodn. of any cytokines by any TCCs. All tested drugs did not suppress the prodn. of cytokines by TCCs from the sarcoidosis patient. These results thus suggest that cytokines produced by T cells infiltrating

in the eye may play an important role in the pathogenesis of uveitis.

IT **104987-11-3**, Tacrolimus
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytokine prodn. by T cells infiltrating in the **eye** of uveitis patients and effects of anti-inflammatory drugs)

L12 ANSWER 15 OF 27 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:712082 HCAPLUS
DOCUMENT NUMBER: 128:30156
TITLE: Cataract development induced by repeated oral dosing with FK506 (tacrolimus) in adult rats
AUTHOR(S): Ishida, Hisao; Mitamura, Takashi; Takahashi, Yuri; Hisatomi, Akihiko; Fukuhara, Yoshifumi; Murato, Kazuo; Ohara, Kaname
CORPORATE SOURCE: Toxicology Research Lab., Fujisawa Pharmaceutical Co. Ltd., Osaka, 532, Japan
SOURCE: Toxicology (1997), 123(3), 167-175
CODEN: TXCYAC; ISSN: 0300-483X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB FK506 (tacrolimus), a potent immunosuppressant, is used for inhibiting allograft rejection in the organ transplantation field. In a preclin. toxicity study in rats, FK506 induced various toxicities, including renal and pancreatic injuries. One of these toxic findings was cataract, and we have found that cataract appeared in rats dosed orally with FK506 for 13 wk and more. Therefore, to better elucidate the onset mechanism of FK506-induced cataract, we measured biochem. parameters, such as sorbitol, Na, K-ATPase and glutathione in the lens of rats. Rats were dosed with FK506 in oral daily doses of 0.2, 1 or 5 mg/kg for 13 wk, the lowest dose of which approximated the expected clin. dosage. Cataract developed in the 5-mg/kg/day group, with an incidence of 25%, whereas no cataract formation was obsd. in the 0.2- or 1-mg/kg/day groups. Five mg/kg/day led an increase of sorbitol and a decrease of reduced type glutathione, but did not affect Na,K-ATPase activity of the lens. FK506 is known to have diabetogenicity through pancreatic injury, which appears as vacuolation of islet cell in rats. Five mg/kg/day of FK506 induced an elevation of blood glucose assocd. with glucose intolerance, and decrease of both basal insulin level and insulin content in the pancreas, and the changes were in parallel with the cataract development in the present study. On the other hand, diabetic parameters did not change in the 0.2- or 1-mg/kg/day groups. These observation suggest that diabetes developed in the rats dosed with 5 mg/kg/day of FK506. Coadministration of a novel aldose reductase inhibitor, Zenarestat, at an oral dose of 50 mg/kg/day resulted in a redn. of incidence of the FK506-induced cataract and a decrease of sorbitol levels in the lens when compared to that in the lens of rats dosed with 5 mg/kg/day of FK506. These results suggest that FK506-induced cataract in rats is due to an accumulation of sorbitol in the lens, secondary to the diabetogenic effect of FK506. FK506 treatment at the doses of 0.2 and 1 mg/kg/day neither affected parameters indicative of diabetes nor induced cataract in rats, suggesting that the cataract would not develop with FK506 if diabetic parameters were kept under control.

IT **104987-11-3**, FK506
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(**eye** sorbitol accumulation in cataract development induced by FK506)

L12 ANSWER 16 OF 27 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:377098 HCAPLUS

DOCUMENT NUMBER: 125:26262
TITLE: Eicosapentaenoic acid and/or docosahexaenoic acid for immunosuppressive therapy of autoimmune eye diseases
INVENTOR(S): Yazawa, Kazuyoshi; Oono, Shigeaki; Ishioka, Misaki; Nakamura, Satoshi
PATENT ASSIGNEE(S): Kanagawa Kagaku Kenkyusho Kk, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08092129	A2	19960409	JP 1993-275999	19931008

PRIORITY APPLN. INFO.: JP 1993-275999 19931008

AB Eicosapentaenoic acid and/or docosahexaenoic acid are claimed for immunosuppressive therapy of autoimmune eye diseases. Thus, patients with uveitis were treated with the oral immunosuppressant FK 506 or cyclosporin A combined with fish oil contg. 6% eicosapentaenoic acid and 25% docosahexaenoic acid with satisfactory results.

IT **104987-11-3**, FK 506
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(eicosapentaenoic acid and/or docosahexaenoic acid for immunosuppressive therapy of autoimmune **eye** diseases)

L12 ANSWER 17 OF 27 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:375747 HCAPLUS
DOCUMENT NUMBER: 125:48727
TITLE: In vitro effects of immunosuppressive agents on cytokine production by HTLV-infected T cell clones derived from the ocular fluid of patients with HTLV-1 uveitis
AUTHOR(S): Sagawa, Kmitaka; Mochizuki, Manabu; Katagiri, Kazuko; Tsuboi, Izumi; Sugita, Sunao; Mukaida, Naofumi; Itoh, Kyogo
CORPORATE SOURCE: Dep. Immunol. Transfusion Med. Ophthalmol., Kurume Univ. Sch. Med., Fukuoka, 830, Japan
SOURCE: Microbiology and Immunology (1996), 40(5), 373-379
CODEN: MIIMDV; ISSN: 0385-5600
PUBLISHER: Center for Academic Publications Japan
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The present study was designed to investigate the in vitro effects of potential therapeutic agents on cytokine prodn. by five HTVL-I-infected T cell clones (TCC) established from the ocular fluid of patients with HTLV-I uveitis. Each of the five HTLV-I-infected TCC was cultured at 1.times.106 cells/mL with or without an immunosuppressive agent (hydrocortisone, FK506, rapamycin, indomethacin, or prostaglandin E2) for 22 h in humidified 5% CO2 in air at 37 C. The prodn. of various cytokines in the culture supernatant from each TCC was measured by ELISA. The HTLV-I-infected TCC produced high amts. of IL-1.alpha., IL-3, IL-6, IL-8, TNF-.alpha., IFN-.gamma., and GM-CSF, and low but significant levels of IL-2 and IL-10 without any stimuli. Hydrocortisone severely depressed the prodn. by these TCC of all the cytokines except for IL-2, which was slightly increased. Prostaglandin E2 depressed the prodn. of IL-1.alpha., while it up-regulated the prodn. of IL-6, TNF-.alpha., and IFN-.gamma.. Rapamycin depressed the prodn. of IL-6 and TNF-.alpha., and FK506 depressed the prodn. of TNF-.alpha.. Hydrocortisone also severely depressed the cytokine prodn. by PHA-stimulated peripheral blood

mononuclear cells obtained from healthy volunteers. Of the immunosuppressive agents tested, hydrocortisone exhibited the strongest suppression of cytokine prodn. by HTLV-I-infected TCC. This result was in agreement with the in vivo effects of hydrocortisone in patients with HTLV-I uveitis. These TCC will be useful in investigating the effects of potential therapeutic agents for HTLV-I uveitis in vitro.

IT **104987-11-3,** FK506
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(In vitro effects of immunosuppressive agents on cytokine prodn. by HTLV-infected T cell clones derived from the **ocular** fluid of patients with HTLV-1 uveitis)

L12 ANSWER 18 OF 27 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:315411 HCAPLUS
DOCUMENT NUMBER: 120:315411
TITLE: Immunosuppressive effect of topical FK506 on penetrating keratoplasty in rats
AUTHOR(S): Hikita, Naofumi
CORPORATE SOURCE: Sch. Med., Kurume Univ., Kurume, 830, Japan
SOURCE: Kurume Igakkai Zasshi (1994), 57(1), 176-89
CODEN: KIZAAL; ISSN: 0368-5810
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB Immunosuppressive effects of topical FK506 on a corneal graft rejection model in allogeneic inbred rats were investigated. Lewis rats were used for recipients and Fisher rats for donors. All rats received i.p. of FK506 (0.3 mg/kg/day) for 7 days in order to ensure baseline parameters. Rats were then assigned randomly to the treatment group (0.3% FK506) and the control (placebo) group. The eyedrops were given every 4 h for 2 wks. Corneal grafts were evaluated with clin. observation, histol. and immunohistol. studies. All the corneal grafts in the control group were rejected by day 14 after surgery while 1/3 of corneal grafts in the treated group survived by day 30 and the difference in the survival rate between the 2 groups was statistically significant ($p < 0.009$) on day 13. The immunohistochem. observations in the FK506-treated corneal grafts were characterized by reduced no. of CD4+ cells and a redn. in the expression of MHC class I antigens and MHC class II antigens and LFA-1. These data suggest that topical FK506 treatment is effective in preventing corneal graft rejection in th Lewis corneal graft model.

IT **104987-11-3,** FK 506
RL: BIOL (Biological study)
(immunosuppressive effect and metab. of, in **eye** corneal allograft)

L12 ANSWER 19 OF 27 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:296631 HCAPLUS
DOCUMENT NUMBER: 120:296631
TITLE: Immunotherapy in ocular diseases
AUTHOR(S): Mochizuki, Manabu
CORPORATE SOURCE: Sch. Med., Kurume Univ., Japan
SOURCE: Nippon Ganka Gakkai Zasshi (1992), 96(12), 1608-34
CODEN: NGZAA6; ISSN: 0029-0203
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB Basic and clin. studies on immunotherapy in immune-mediated ocular disorders, i.e. uveitis, allograft rejection in corneal transplantation and allergic conjunctivitis, were carried out using a variety of immunosuppressants, including immunophilin ligands (FK506 and cyclosporine). In an animal model for uveitis, exptl. autoimmune uveitis

(EAU), immunophilin ligands were demonstrated in the rat and monkey to have unique immunol. activities : (1) intense and prolonged suppression of EAU development, (2) therapeutic effects by treating animals only after disease onset, (3) selective suppression on cellular immune response to S-antigen, (4) induction of immunol. tolerance and activation of antigen specific suppressor cells. Combination therapy with low doses of immunophilin ligand and other immunosuppressants was tested to achieve better effects with less side effects. A low dose of cyclosporine (2 mg/kg/day) with bucillamine (20 mg/kg/day) which suppresses antigen-presenting activity by macrophages caused much stronger suppression of EAU than the therapy with either cyclosporine or bucillamine alone. Similarly, a low dose of FK506 (0.1 mg/kg/day) with dexamethasone (0.01 mg/kg/day) caused stronger suppression of EAU. A multi-center clin. open trial of FK506 in refractory uveitis was carried out in Japan. A total of 40 cases of active uveitis in the posterior segment of the eye were treated with FK506 (0.05, 0.1 or 0.2 mg/kg/day) and the mean observation period was 26.2 wk. FK506 therapy improved uveitis in 60% of all cases including 47% of patients resistant to previous therapy with cyclosporine. FK506 significantly suppressed the no. of uveitis attacks in patients with Behcet's disease. As for the side effects, 22.5% of patients showed abnormal values of renal function on FK506. The trough level of FK506 in whole blood correlated with adverse side effects as well as with therapeutic effect on uveitis, and it should be maintained between 15 and 25 ng/mL. Studies with immunophilin ligands indicate that they are beneficial for the therapy of severe allergic conjunctivitis and for treatment of allograft rejection.

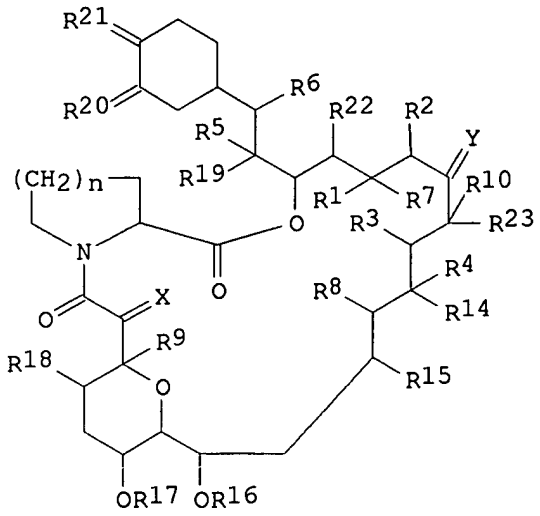
IT **104987-11-3**, FK506
RL: BIOL (Biological study)
(in **ocular** disease and corneal allograft treatment)

L12 ANSWER 20 OF 27 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:45786 HCAPLUS
DOCUMENT NUMBER: 118:45786
TITLE: Use of macrolide compounds for eye diseases, especially allergic conjunctivitis
INVENTOR(S): Mochizuki, Manabu; Iwaki, Yoichi
PATENT ASSIGNEE(S): Kurume University, Japan
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9219278	A1	19921112	WO 1992-JP545	19920424
W: CA, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
CA 2102241	AA	19921027	CA 1992-2102241	19920424
EP 581959	A1	19940209	EP 1992-909558	19920424
EP 581959	B1	20010117		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 07500570	T2	19950119	JP 1992-508698	19920424
JP 3158437	B2	20010423		
AT 198708	E	20010215	AT 1992-909558	19920424
ES 2154262	T3	20010401	ES 1992-909558	19920424
US 5514686	A	19960507	US 1994-133194	19940401

PRIORITY APPLN. INFO.:
GB 1991-9060 A 19910426
GB 1991-21661 A 19911011
WO 1992-JP545 W 19920424

OTHER SOURCE(S): MARPAT 118:45786
GI



I

AB Macrolides I [each pair of vicinal substituents (R1 and R2, R3 and R4, R6 and R6) = H pair or bond, R2 may also be alkyl; R7 = H, (protected) OH, alkoxy, or (with R1) :O; R8, R9 = H, OH; R10 = H, (hydroxy-substituted or :O-substituted) alkyl, (hydroxy-substituted) alkenyl; X = O, (H,OH), (H,H), CH2O; Y = O, (H,OH), (H,H), NNR11R12, NOR13 (R11, R12 = H, alkyl, aryl, tosyl; R13 = H, alkyl); R14-R19, R22, R23 = H, alkyl; R20, R21 = O, (R20a,H), (R21a,H) (R20a, R21a = OH, alkoxy, OCH2OCH2CH2OCH3, or R21a is protected OH, or R20a and R21a together are epoxide ring O); n = 1-3; Y, R10, R23 (with C to which they are attached) may also be 5- or 6-membered N- or S- or O-contg. (un)satd. (substituted) heterocyclyl], and pharmaceutically acceptable salts thereof, are disclosed for prevention or treatment of allergic conjunctivitis. Capsule and eye drop formulations of FK 506 are presented, as is the effect of FK 506 on passive anaphylaxis in rat conjunctiva..

IT **104987-11-3**, FK 506
RL: BIOL (Biological study)
(**eye** drops and capsules of, for allergic conjunctivitis treatment)

L12 ANSWER 21 OF 27 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1992:455982 HCAPLUS
DOCUMENT NUMBER: 117:55982
TITLE: Suspensions containing tricyclic or related compounds for oral or ocular use
INVENTOR(S): Asakura, Sotoo; Koyama, Yasuto; Kiyota, Youhei; Akashi, Kiyoko; Kagayama, Akira; Murakami, Yoshio; Nakate, Toshiomi
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

EP 484936	A1	19920513	EP 1991-118982	19911107
EP 484936	B1	19941005		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
CA 2054983	AA	19920509	CA 1991-2054983	19911105
RU 2079304	C1	19970520	RU 1991-5010186	19911106
AU 9187099	A1	19920514	AU 1991-87099	19911107
AU 653556	B2	19941006		
ZA 9108846	A	19920826	ZA 1991-8846	19911107
HU 60925	A2	19921130	HU 1991-3507	19911107
HU 210760	B	19950728		
ES 2061149	T3	19941201	ES 1991-118982	19911107
CN 1061907	A	19920617	CN 1991-110733	19911108
CN 1069195	B	20010808		
JP 05155770	A2	19930622	JP 1991-293148	19911108
JP 2581359	B2	19970212		
IL 100011	A1	19951208	IL 1991-100011	19911108
US 5368865	A	19941129	US 1993-97617	19930727
US 5496564	A	19960305	US 1994-296403	19940826

PRIORITY APPLN. INFO.:

JP 1990-304839	A	19901108
GB 1991-4834	A	19910307
JP 1991-259358	A	19911007
US 1991-788041	B1	19911105
US 1993-97617	A1	19930727

OTHER SOURCE(S): MARPAT 117:55982

AB A tricyclic compd. such as FK 506 or related compds. (Markush included) is made into suspension by addn. of a surfactant, e.g. a polyoxyethlene sorbitan fatty acid ester. The compn. can be used as an orally administrable agent or eye drops. Formulations contg. FK 506 are given, and absorption tests (for eye drop and oral compns.) are reported.

IT **104987-11-3**, FK 506 **104987-12-4**
RL: BIOL (Biological study)
(oral or **ocular** pharmaceutical suspension of)

L12 ANSWER 22 OF 27 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1992:75881 HCAPLUS
DOCUMENT NUMBER: 116:75881
TITLE: Effect of FK-506 on corneal allograft survival in the rabbit
AUTHOR(S): Kobayashi, Chihiro; Kanai, Atsushi; Nakajima, Akira
CORPORATE SOURCE: Sch. Med., Juntendo Univ., Tokyo, 113, Japan
SOURCE: Atarashii Ganka (1991), 8(11), 1771-4
CODEN: ATGAEX; ISSN: 0910-1810
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB To assess the efficacy of subconjunctivally injected FK-506 in suppressing corneal graft rejection, rabbit corneal allograft transplantation was carried out. When rekeratoplasty was performed in rabbits treated with FK-506 (0.1 mg/kg, twice a wk, for 14 wk), 8/11 were successfully transplanted and 7 of the 8 corneas kept transparency on 100th day. After exchange keratoplasties with FK-506 (0.01 mg/kg, once a wk, for 14 wk), 9/10 were successfully transplanted and all of the 9 corneas kept transparency on 200th day. When FK-506 (0.1 mg/kg) injected subconjunctivally, the concn. in anterior chamber was highest 8 h after the injection.

IT **104987-11-3**, FK-506
RL: BIOL (Biological study)
(**eye** corneal transplant survival increase by subconjunctival)

L12 ANSWER 23 OF 27 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1992:15272 HCAPLUS

DOCUMENT NUMBER: 116:15272
TITLE: Cornea and aqueous humor permeability to FK-506 eyedrops
AUTHOR(S): Akiyama, Shuichi; Yokoyama, Toshiyuki; Kobayashi, Chihiro; Kanai, Atsushi; Kagayama, Akira
CORPORATE SOURCE: Sch. Med., Juntendo Univ., Tokyo, 113, Japan
SOURCE: Atarashii Ganka (1991), 8(9), 1445-8
CODEN: ATGAEX; ISSN: 0910-1810
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB The soln,. of FK-506, a macrolide antibiotic as an immunosuppressant isolated form Streptocmyces, was instilled in the eyes of rabbit 10 times at 30 min intervals. No remarkable stimulant effect was detected by the Draize method. In this expt., FGK-506 was found in the cornea and iris in concns. of 944 and 930 ng/g, resp.
IT **104987-11-3**, FK 506
RL: BIOL (Biological study)
(of **eye** compns., after **eyedrop** instillation)

L12 ANSWER 24 OF 27 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:150214 HCAPLUS
DOCUMENT NUMBER: 114:150214
TITLE: Aqueous liquid compositions containing dioxaazatricyclooctacosenetetraones
INVENTOR(S): Honbo, Toshiyasu; Tanimoto, Sachiyo; Yoshida, Hiromitsu; Hata, Takehisa; Asakura, Sotoo; Koyama, Yasuto; Kiyota, Youhei
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 406791	A2	19910109	EP 1990-112655	19900703
EP 406791	A3	19911106		
EP 406791	B1	19950201		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AU 9058642	A1	19910124	AU 1990-58642	19900703
AU 635286	B2	19930318		
ZA 9005202	A	19910424	ZA 1990-5202	19900703
ES 2066915	T3	19950316	ES 1990-112655	19900703
CA 2020431	AA	19910106	CA 1990-2020431	19900704
IL 94971	A1	19951208	IL 1990-94971	19900704
CN 1048496	A	19910116	CN 1990-103445	19900705
CN 1063322	B	20010321		
JP 03128320	A2	19910531	JP 1990-178974	19900705
JP 2536248	B2	19960918		
US 5770607	A	19980623	US 1994-276495	19940718

PRIORITY APPLN. INFO.: JP 1989-176637 A 19890705
US 1990-546883 B1 19900702
US 1992-853020 B1 19920318
OTHER SOURCE(S): MARPAT 114:150214
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB An aq. compn., such as eye drop comprises the title compds. [I; R1-R6 = H or R1R2, R3R4, and R5R6 forming bonds or R2 = alkyl; H, OH, protected OH, alkoxy or R1R7 = O; R8, R9 = OH; R10 = H, (un)substituted alkyl, etc.; X = O, CH2O, (H,OH), (H,H); Y = O, (H,OH), (H,H), NNR11R12, NOR13, etc.; R11, R12 = H, alkyl, aryl, tosyl; R13 - R19, R22, R23 = H, alkyl; R20, R21 = O, (OH, H), (alkoxy, H), etc.; n = 1-3] and a solubilizer, such as cellulose derivs. I have immunosuppressive and antimicrobial activities (no data given). An aq. eye drop contained FK 506 (II) 100, hydroxypropyl Me cellulose 350, Na2HPO4 18.4, NaH2PO4 1547, phosphate 0.32, NaCl 288, benzalkonium chloride 20 mg, and water to 100 mL.

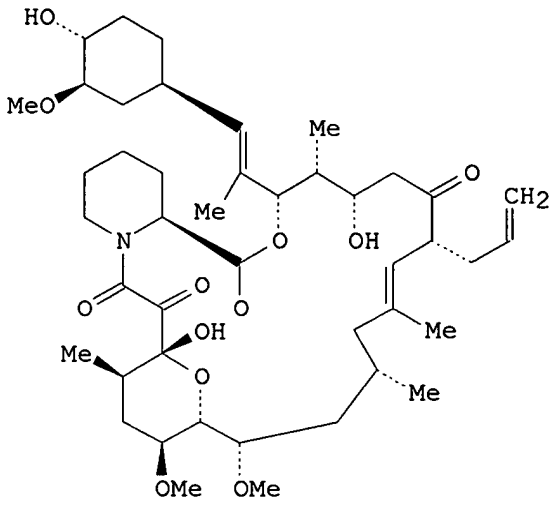
IT **104987-11-3**, FK 506
RL: BIOL (Biological study)
(**eye** drops contg.)

L12 ANSWER 25 OF 27 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:55455 HCAPLUS
DOCUMENT NUMBER: 114:55455
TITLE: Effects of FK-506 and cyclosporin A on the survival of corneal grafts in rabbits
AUTHOR(S): Kobayashi, Chihiro
CORPORATE SOURCE: Sch. Med., Juntendo Univ., Tokyo, 113, Japan
SOURCE: Juntendo Igaku (1990), 36(2), 189-96
CODEN: JUIZAG; ISSN: 0022-6769
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB The effects on subconjunctival injection of FK-506 and cyclosporin A eyedrops after corneal allograft transplant surgery are described. In rabbits treated with FK-506, the survival rate after exchange keratoplasty (0.1 mg/kg, twice a week) was 100% on day 100 after re-keratoplasty (0.1 mg/kg, twice a week) 88% on day 100 and after exchange keratoplasty (0.01 mg/kg, once a week) 100% on day 200. In rabbits treated with cyclosporin A, the survival rate after exchange keratoplasty (0.025%, 4 times a day) was 100% on day 100 and after re-keratoplasty (0.025%, 4 times a day) 66% on day 40.

IT **104987-11-3**, FK-506
RL: BIOL (Biological study)
(**eye** cornea transplant survival increase by)

L12 ANSWER 26 OF 27 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1989:489968 HCAPLUS
DOCUMENT NUMBER: 111:89968
TITLE: Suppression of corneal graft rejection in rabbits by a new immunosuppressive agent, FK-506
AUTHOR(S): Kobayashi, C.; Kanai, A.; Nakajima, A.; Okumura, K.
CORPORATE SOURCE: Dep. Ophthalmol., Juntendo Univ., Tokyo, 113, Japan
SOURCE: Transplantation Proceedings (1989), 21(1, Book 3), 3156-8
CODEN: TRPPA8; ISSN: 0041-1345
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB In rabbits with corneal grafts, topical administration of FK-506 (I) by subconjunctival injection inhibited the allograft rejection. In addn., I showed no occular toxicity.

IT **104987-11-3**, FK-506
RL: BIOL (Biological study)
(**eye** cornea graft rejection inhibition by)

L12 ANSWER 27 OF 27 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1988:431719 HCAPLUS
DOCUMENT NUMBER: 109:31719
TITLE: Effect of FK-506 on the survival of corneal grafts in rabbits
AUTHOR(S): Kobayashi, Chihiro; Kanai, Atsushi; Shu, Shityu; Nakajima, Akira; Okumura, Ko; Iwasaki, Kazuhide
CORPORATE SOURCE: Sch. Med., Juntendo Univ., Tokyo, 113, Japan
SOURCE: Atarashii Ganka (1988), 5(2), 277-80
CODEN: ATGAEX; ISSN: 0910-1810
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB The survival rates of grafts in the treated and control groups 100 days after surgery were 100% and 25%, resp. No toxicity attributable to the drug was obsd.

IT **104987-11-3**, FK 506
RL: BIOL (Biological study)
(**eye** cornea transplant survival response to)

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E1 THROUGH E12 ASSIGNED

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FILE 'REGISTRY' ENTERED AT 12:03:47 ON 26 FEB 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 25 FEB 2003 HIGHEST RN 494824-56-5
DICTIONARY FILE UPDATES: 25 FEB 2003 HIGHEST RN 494824-56-5

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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L13  ANSWER 1 OF 12  REGISTRY  COPYRIGHT 2003 ACS
RN   491875-86-6  REGISTRY
CN   Hydrazinecarboxylic acid, [(3S,4R,5S,8R,9E,12S,14S,15R,16S,18R,19R,26aS)-
     1,3,4,5,6,8,11,12,13,14,15,16,17,18,19,20,21,23,24,25,26,26a-docosahydro-
     5,19-dihydroxy-3-[(1E)-2-[(1R,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-
     methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-1,20,21-trioxo-8-(2-
     propenyl)-15,19-epoxy-7H-pyrido[2,1-c][1,4]oxaazacyclotricosin-7-ylidene]-
     , 2-(2-pyridinyldithio)ethyl ester (9CI)  (CA INDEX NAME)
FS   STEREOSEARCH
MF   C52 H78 N4 O13 S2
SR   CA
LC   STN Files:   CAPLUS
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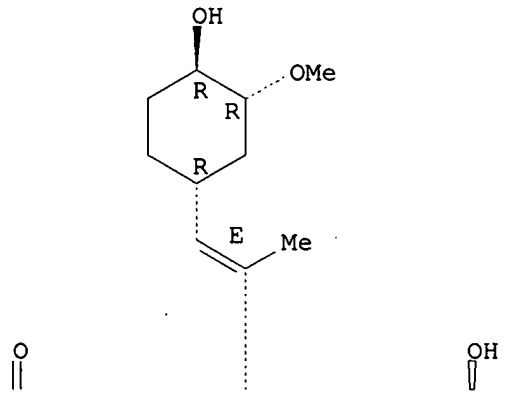
Absolute stereochemistry.
Double bond geometry as described by E or Z.

PAGE 1-A



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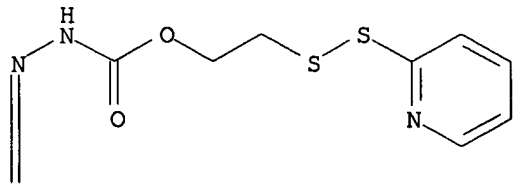

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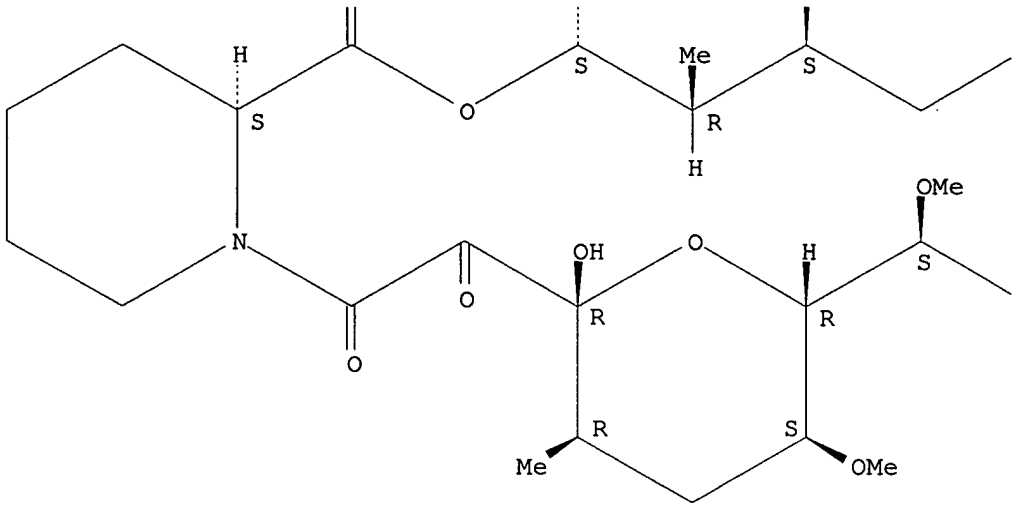

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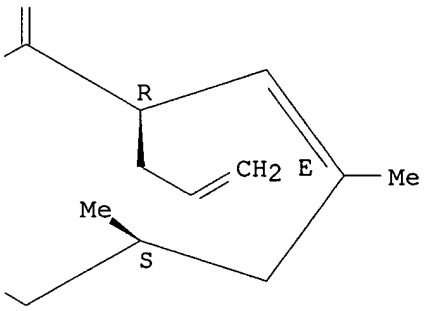


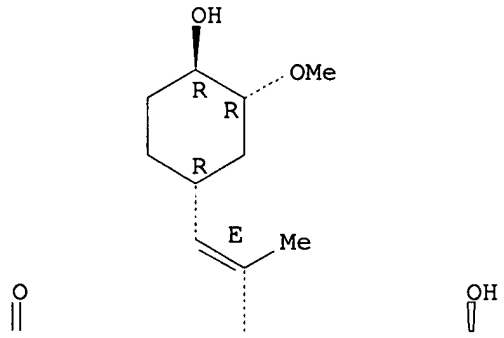
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

L13 ANSWER 2 OF 12 REGISTRY COPYRIGHT 2003 ACS
RN **491875-85-5** REGISTRY
CN INDEX NAME NOT YET ASSIGNED
FS STEREOSEARCH
MF C54 H82 N4 O14
SR CA
LC STN Files: CAPLUS

Absolute stereochemistry.
Double bond geometry as described by E or Z.

PAGE 1-A



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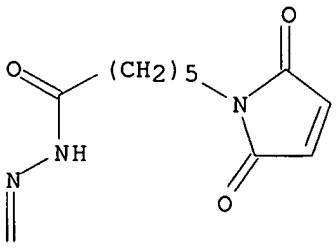

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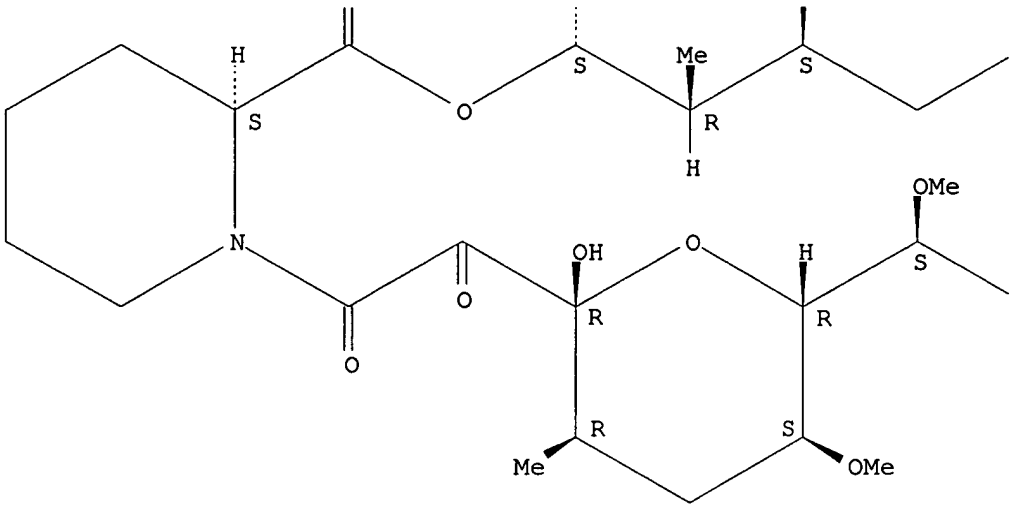

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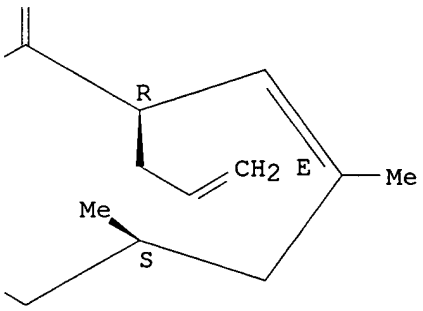

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

L13 ANSWER 3 OF 12 REGISTRY COPYRIGHT 2003 ACS
RN **491875-84-4** REGISTRY
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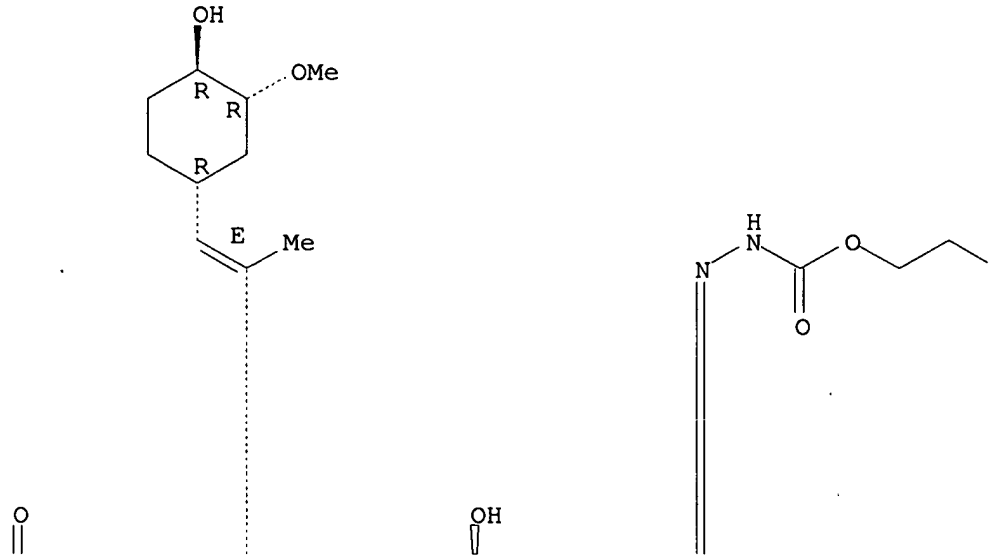
FS STEREOSEARCH
MF C92 H165 N33 O21 S2
SR CA
LC STN Files: CAPLUS

Absolute stereochemistry.
Double bond geometry as described by E or Z.

PAGE 1-B



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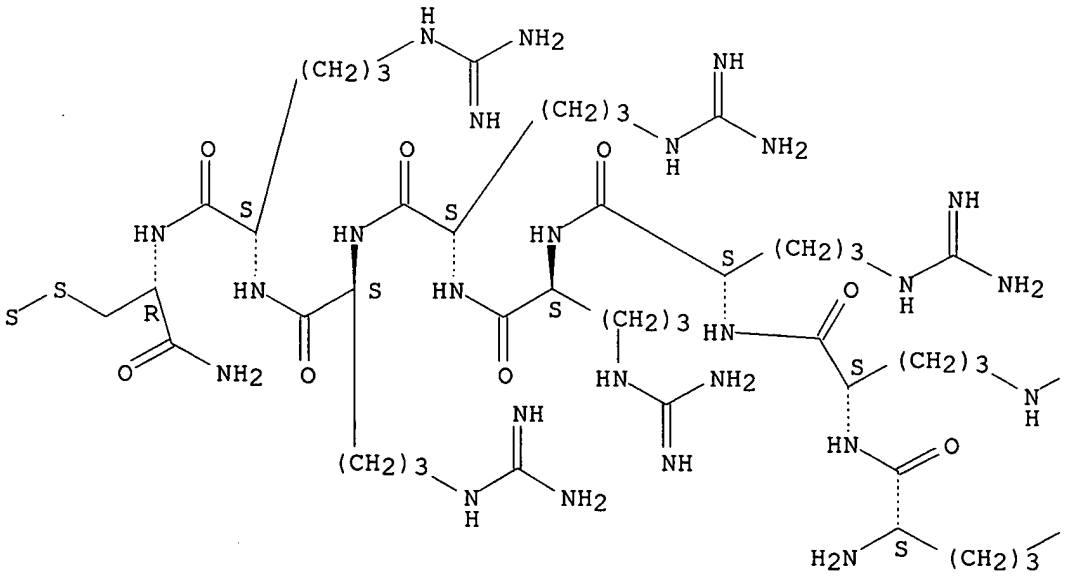

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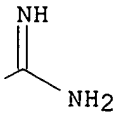

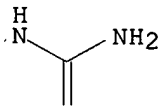

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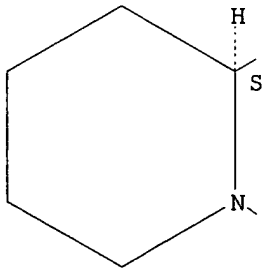

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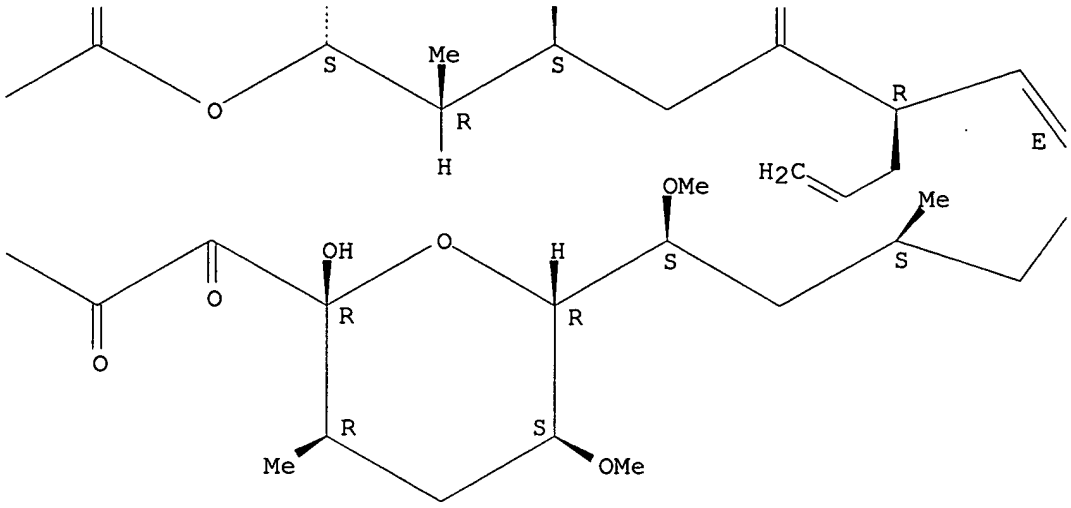

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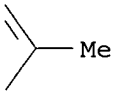

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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

L13 ANSWER 4 OF 12 REGISTRY COPYRIGHT 2003 ACS
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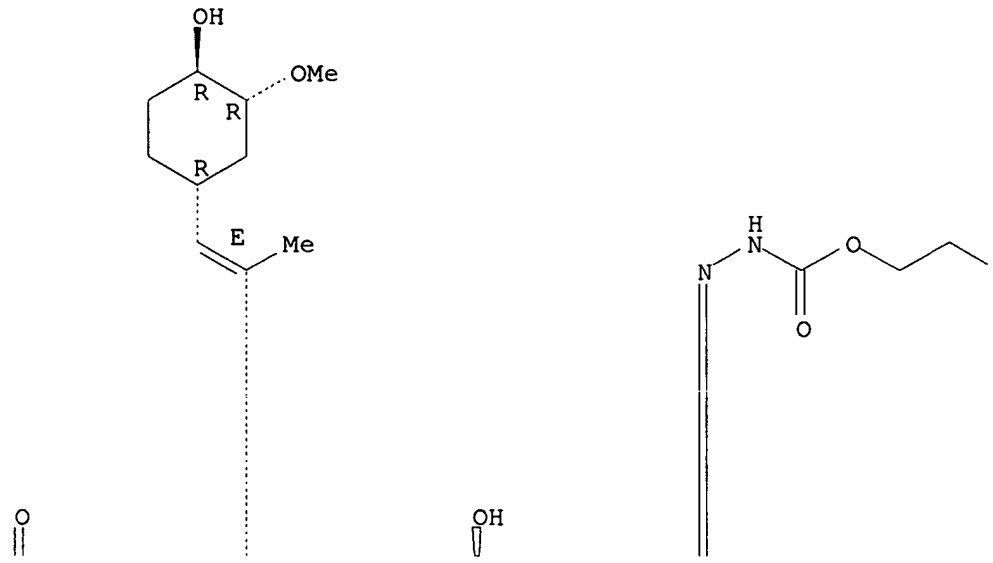
FS STEREOSEARCH
MF C92 H165 N33 O21 S2
SR CA
LC STN Files: CAPLUS

Absolute stereochemistry.

Double bond geometry as described by E or Z.

PAGE 1-B



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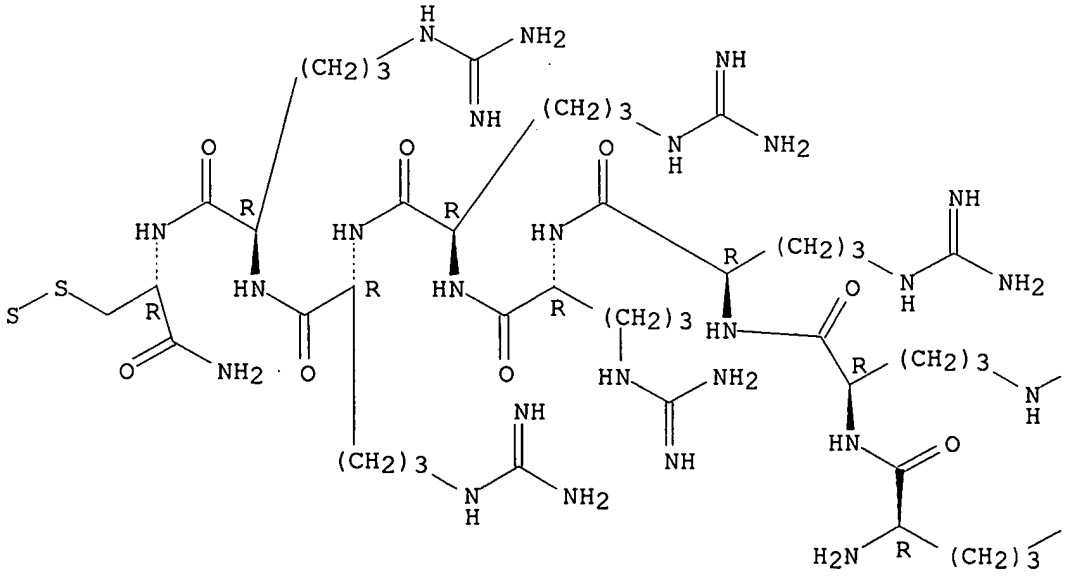

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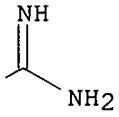

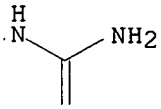

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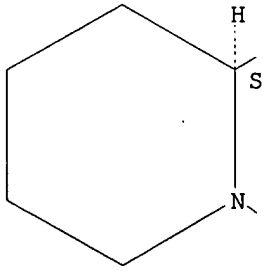

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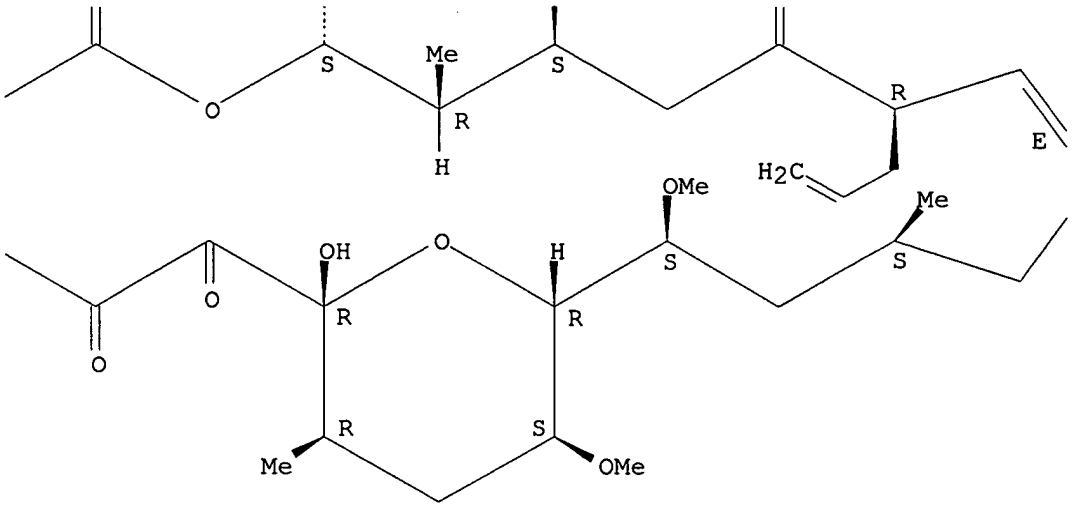

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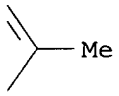

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L13 ANSWER 5 OF 12 REGISTRY COPYRIGHT 2003 ACS
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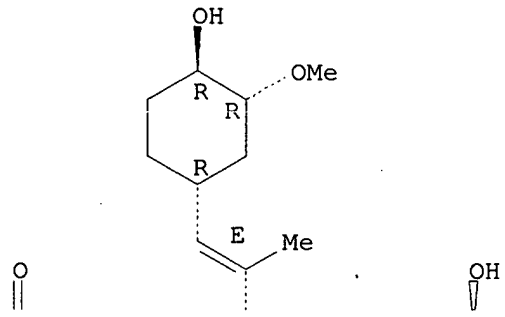
FS STEREOSEARCH
MF C99 H174 N34 O22 S
SR CA
LC STN Files: CAPLUS

Absolute stereochemistry.
Double bond geometry as described by E or Z.

PAGE 1-A



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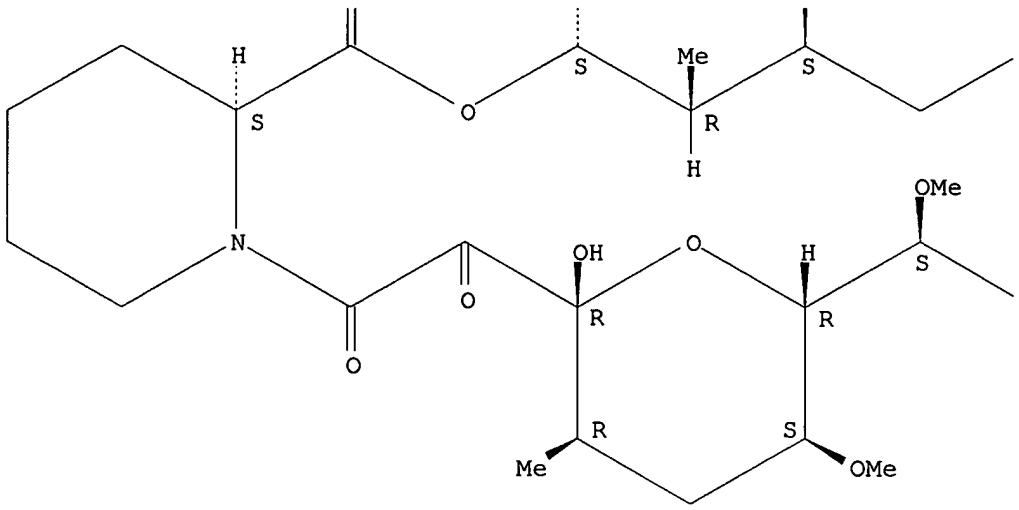

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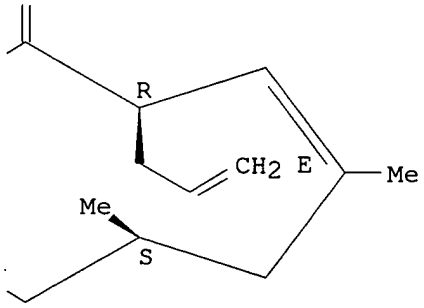

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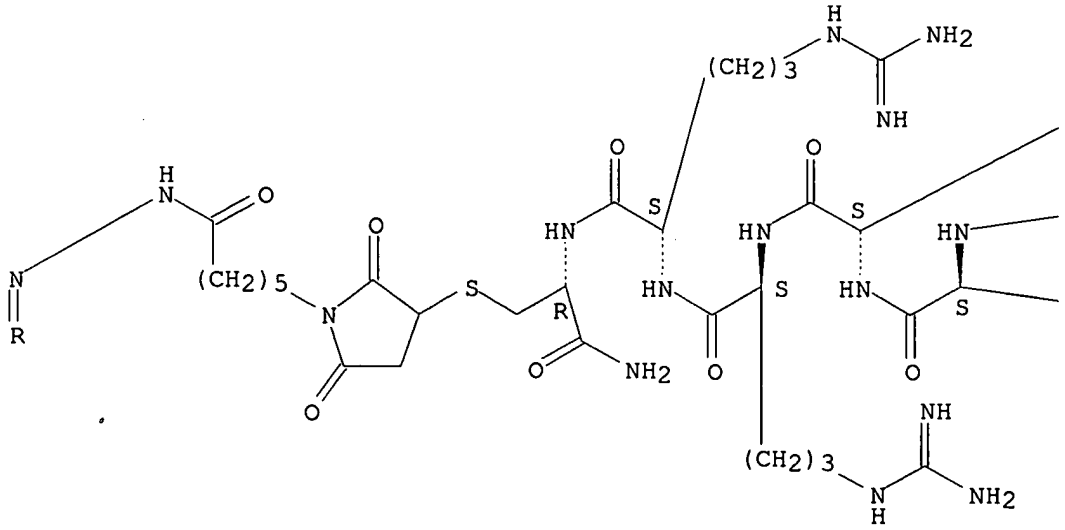

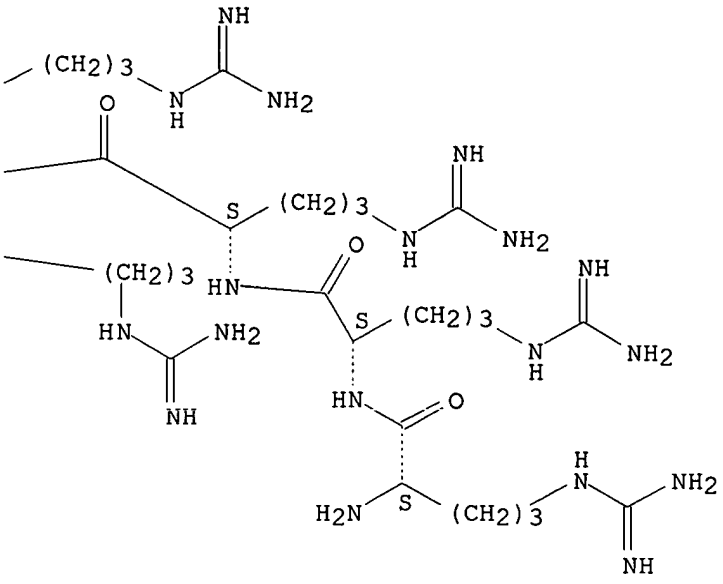

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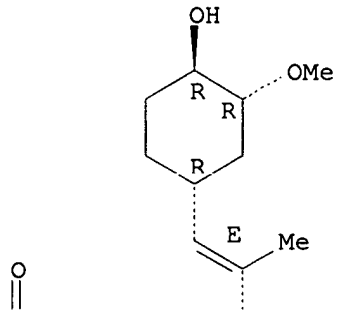
L13 ANSWER 6 OF 12 REGISTRY COPYRIGHT 2003 ACS
RN **491875-81-1** REGISTRY
CN L-Cysteinamide, D-arginyl-D-arginyl-D-arginyl-D-arginyl-D-arginyl-D-arginyl-D-arginyl-S-[1-[6-[[(3S,4R,5S,8R,9E,12S,14S,15R,16S,18R,19R,26aS)-1,3,4,5,6,8,11,12,13,14,15,16,17,18,19,20,21,23,24,25,26,26a-docosahydro-5,19-dihydroxy-3-[(1E)-2-[(1R,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-1,20,21-trioxo-8-(2-propenyl)-15,19-epoxy-7H-pyrido[2,1-c][1,4]oxaazacyclotricosin-7-ylidene]hydrazino]-6-oxohexyl]-2,5-dioxo-3-pyrrolidinyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C99 H174 N34 O22 S
SR CA
LC STN Files: CAPLUS

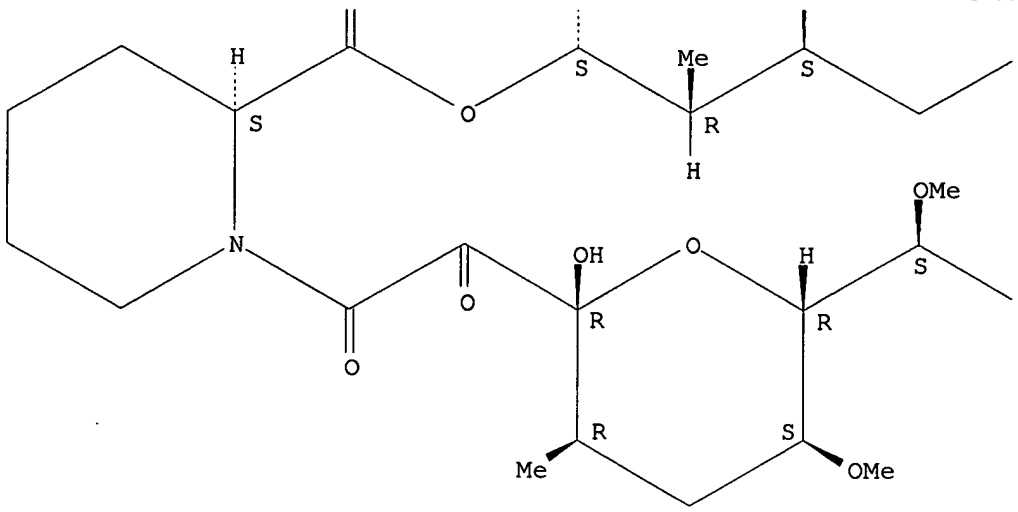
Absolute stereochemistry.
Double bond geometry as described by E or Z.

PAGE 1-A



PAGE 1-B

PAGE 2-A



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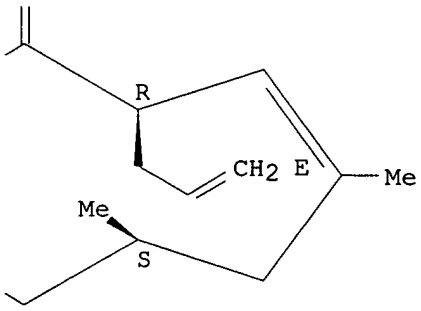

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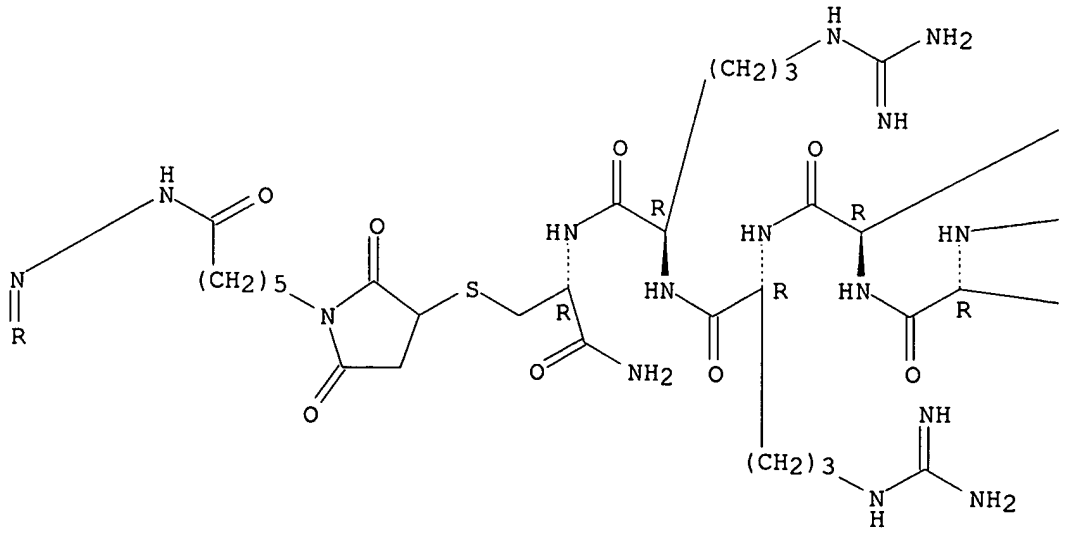
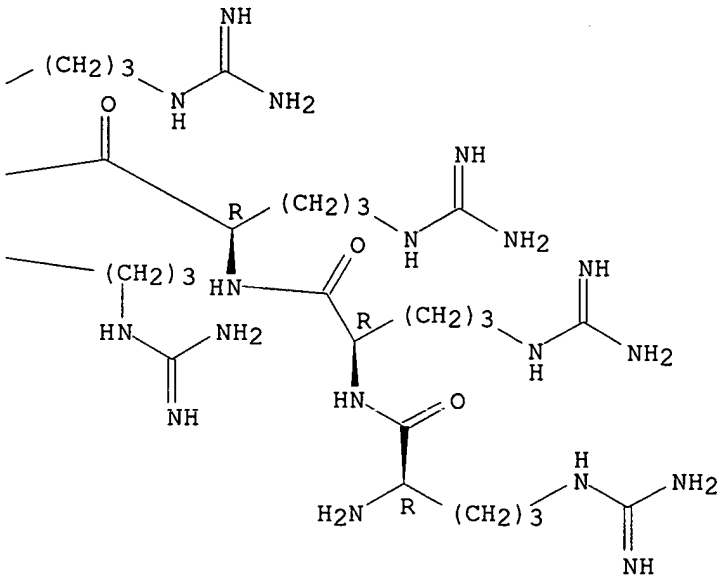




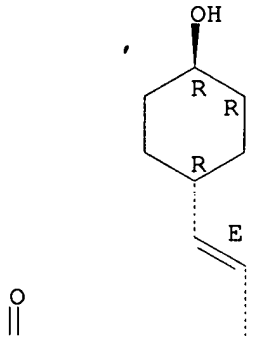
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

L13 ANSWER 7 OF 12 REGISTRY COPYRIGHT 2003 ACS
RN **491875-80-0** REGISTRY
CN INDEX NAME NOT YET ASSIGNED
FS STEREOSEARCH
MF C73 H115 N9 O18 S2
SR CA
LC STN Files: CAPLUS

Absolute stereochemistry.
Double bond geometry as described by E or Z.

PAGE 1-A



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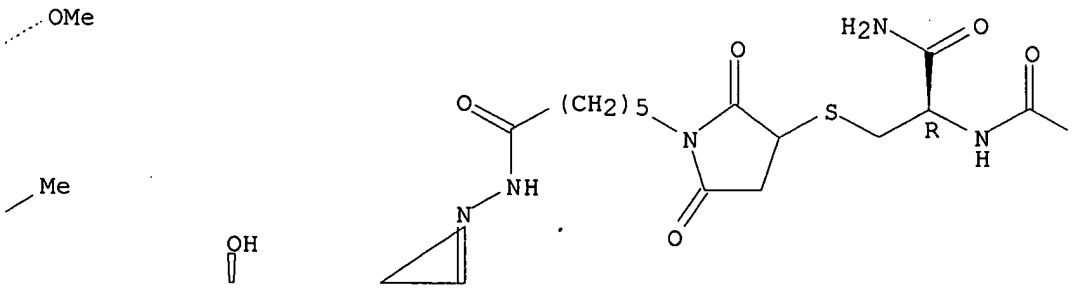

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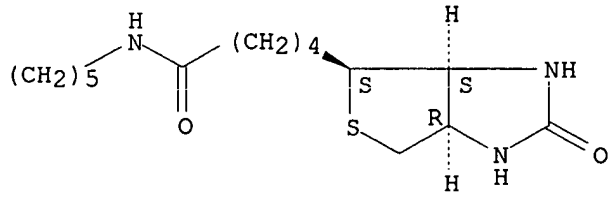

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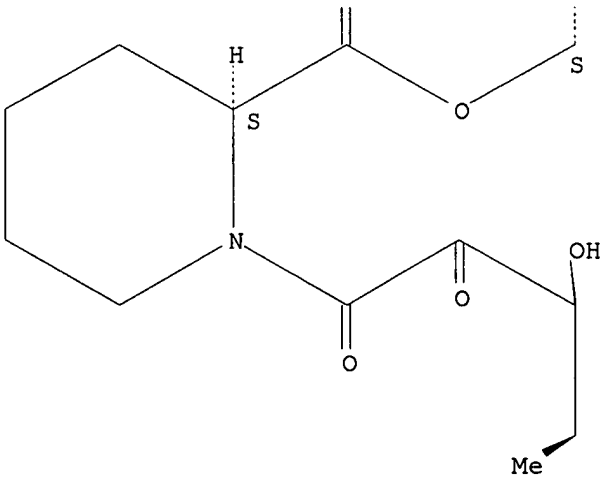
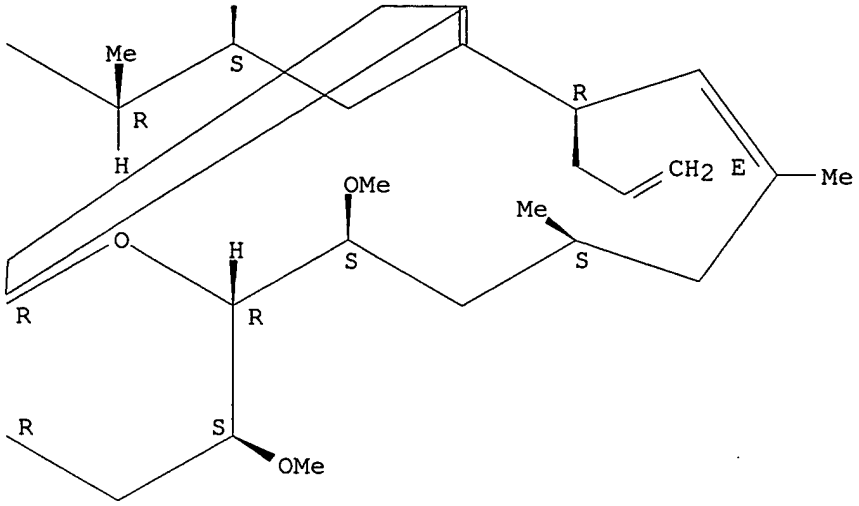




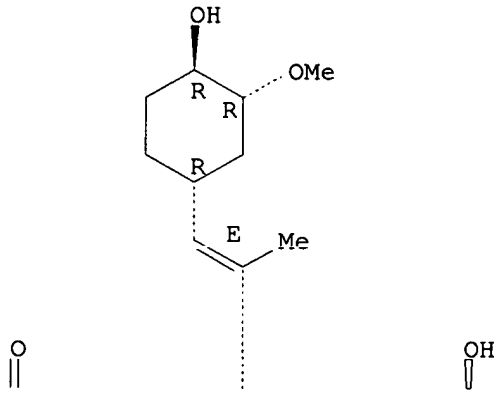
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

L13 ANSWER 8 OF 12 REGISTRY COPYRIGHT 2003 ACS
RN **491875-79-7** REGISTRY
CN L-Cysteinamide, N2-[6-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]amino]-1-oxohexyl]-D-arginyl-D-arginyl-D-arginyl-D-arginyl-D-arginyl-D-arginyl-D-arginyl-S-[1-[6-[[(3S,4R,5S,8R,9E,12S,14S,15R,16S,18R,19R,26aS)-1,3,4,5,6,8,11,12,13,14,15,16,17,18,19,20,21,23,24,25,26,26a-docosahydro-5,19-dihydroxy-3-[(1E)-2-[(1R,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-1,20,21-trioxo-8-(2-propenyl)-15,19-epoxy-7H-pyrido[2,1-c][1,4]oxaazacyclotricosin-7-ylidene]hydrazino]-6-oxohexyl]-2,5-dioxo-3-pyrrolidinyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C115 H199 N37 O25 S2
SR CA
LC STN Files: CAPLUS

Absolute stereochemistry.
Double bond geometry as described by E or Z.

PAGE 1-A



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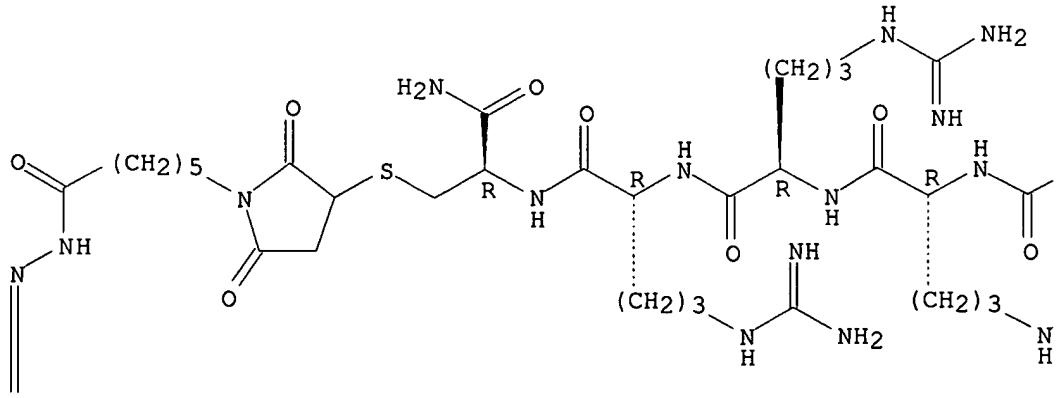
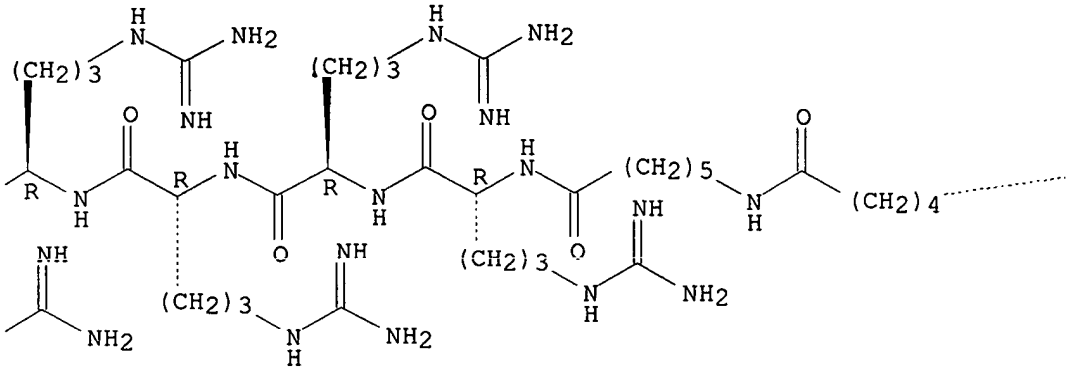


PAGE 1-C



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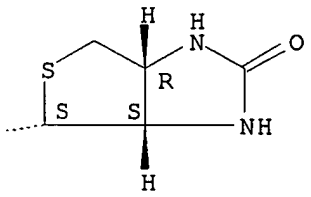

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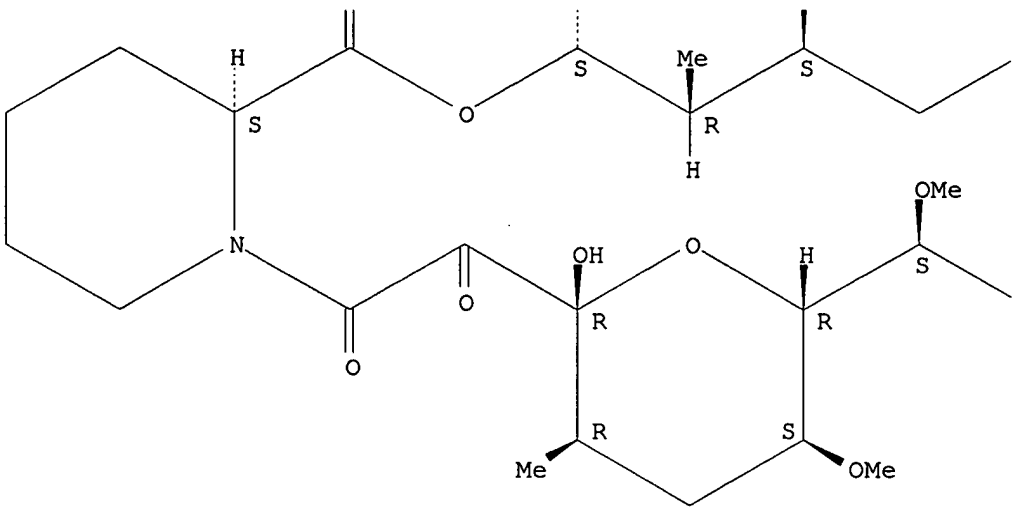

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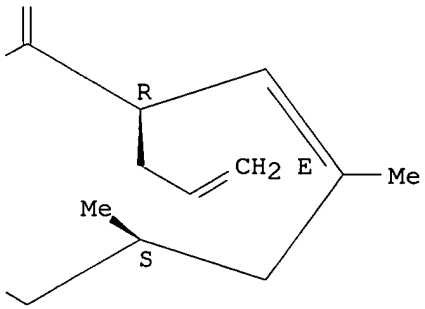


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

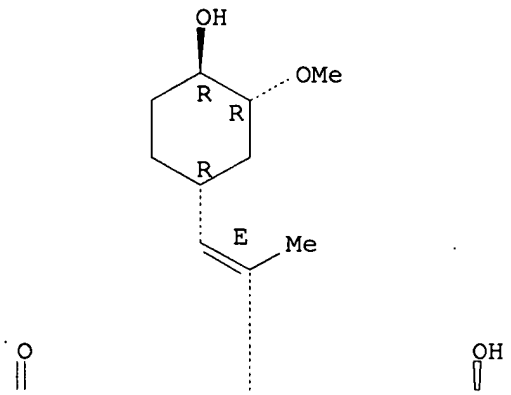
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

L13 ANSWER 9 OF 12 REGISTRY COPYRIGHT 2003 ACS
RN **491875-78-6** REGISTRY
CN L-Cysteinamide, N2-[6-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]amino]-1-oxohexyl]-D-arginyl-D-arginyl-D-arginyl-D-arginyl-D-arginyl-D-arginyl-D-arginyl-D-arginyl-S-[1-[6-[[(3S,4R,5S,8R,9E,12S,14S,15R,16S,18R,19R,26aS)-1,3,4,5,6,8,11,12,13,14,15,16,17,18,19,20,21,23,24,25,26,26a-docosahydro-5,19-dihydroxy-3-[(1E)-2-[(1R,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-1,20,21-trioxo-8-(2-propenyl)-15,19-epoxy-7H-pyrido[2,1-c][1,4]oxaazacyclotricosin-7-ylidene]hydrazino]-6-oxohexyl]-2,5-dioxo-3-pyrrolidinyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C127 H223 N45 O27 S2
SR CA
LC STN Files: CAPLUS

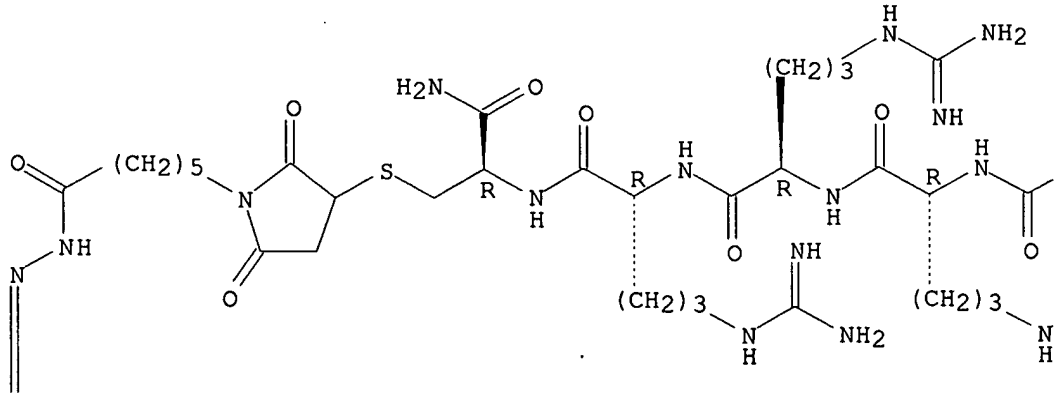
Absolute stereochemistry.

Double bond geometry as described by E or Z.

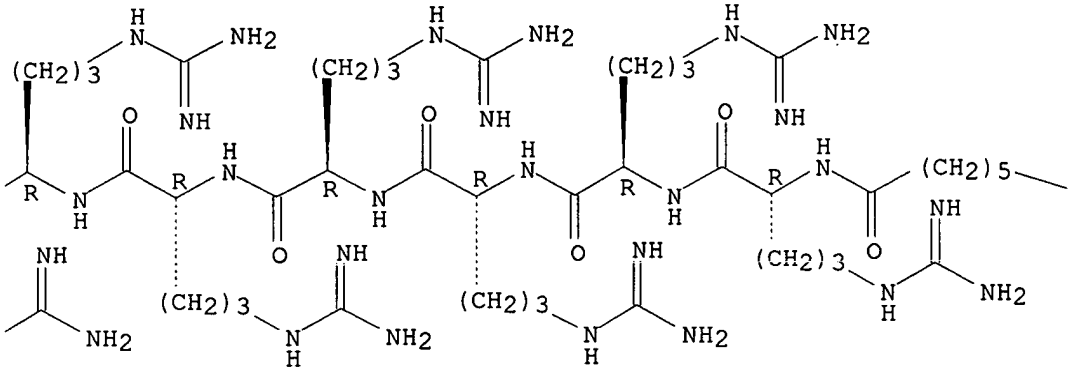
PAGE 1-A



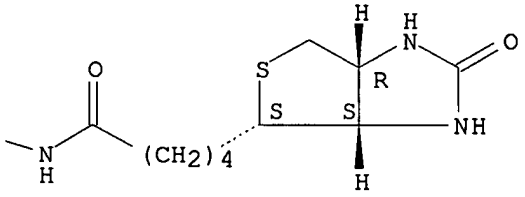
PAGE 1-B



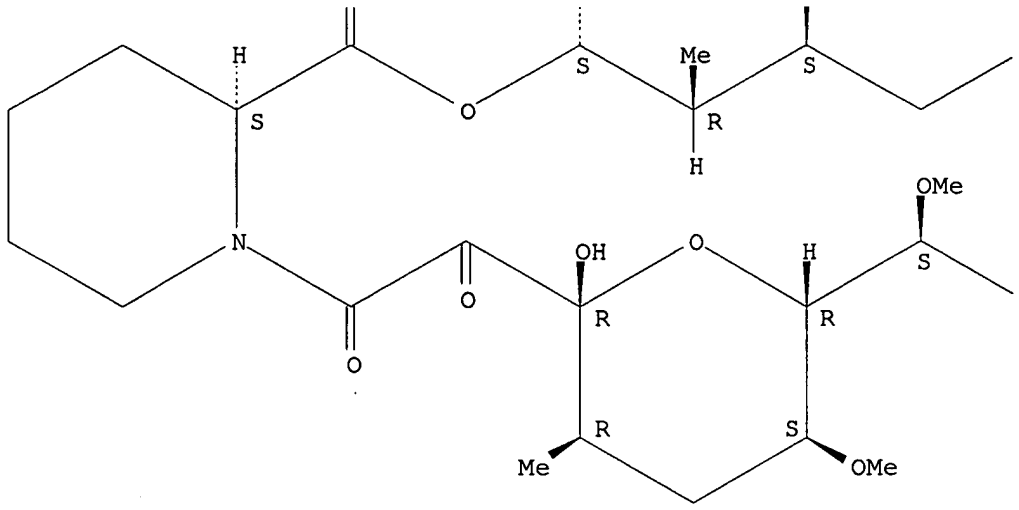
PAGE 1-C



PAGE 1-D



PAGE 2-A



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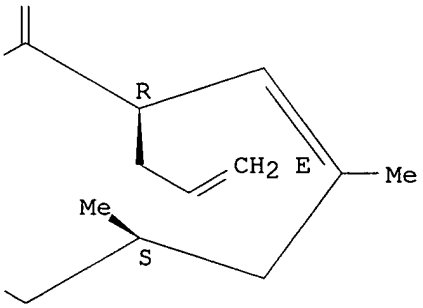


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

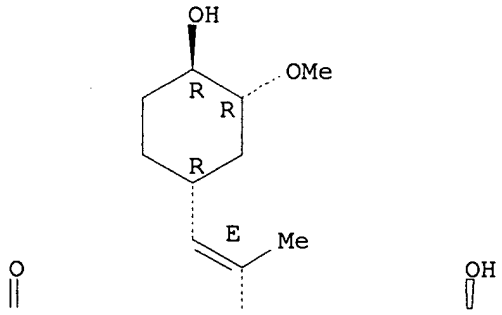
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

L13 ANSWER 10 OF 12 REGISTRY COPYRIGHT 2003 ACS
RN **109581-93-3** REGISTRY
CN 15,19-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosine-1,7,20,21(4H,23H)-tetrone, 5,6,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-5,19-dihydroxy-3-[(1E)-2-[(1R,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-8-(2-propenyl)-, monohydrate, (3S,4R,5S,8R,9E,12S,14S,15R,16S,18R,19R,26aS)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 15,19-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosine-1,7,20,21(4H,23H)-tetrone, 5,6,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-5,19-dihydroxy-3-[2-(4-hydroxy-3-methoxycyclohexyl)-1-methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-8-(2-propenyl)-, monohydrate, [3S-[3R*[E(1S*,3S*,4S*)],4S*,5R*,8S*,9E,12R*,14R*,15S*,16R*,18S*,19S*,26aR*]]-
OTHER NAMES:
CN Tacrolimus hydrate
CN Tsukubaenolide hydrate

FS STEREOSEARCH
MF C44 H69 N O12 . H2 O
SR CA
LC STN Files: ADISINSIGHT, BIOSIS, CA, CANCERLIT, CAPLUS, CHEMCATS, CIN, CSCHEM, DRUGPAT, DRUGUPDATES, IPA, MEDLINE, PROMT, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPATFULL
(*File contains numerically searchable property data)
CRN (104987-11-3)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

PAGE 1-A



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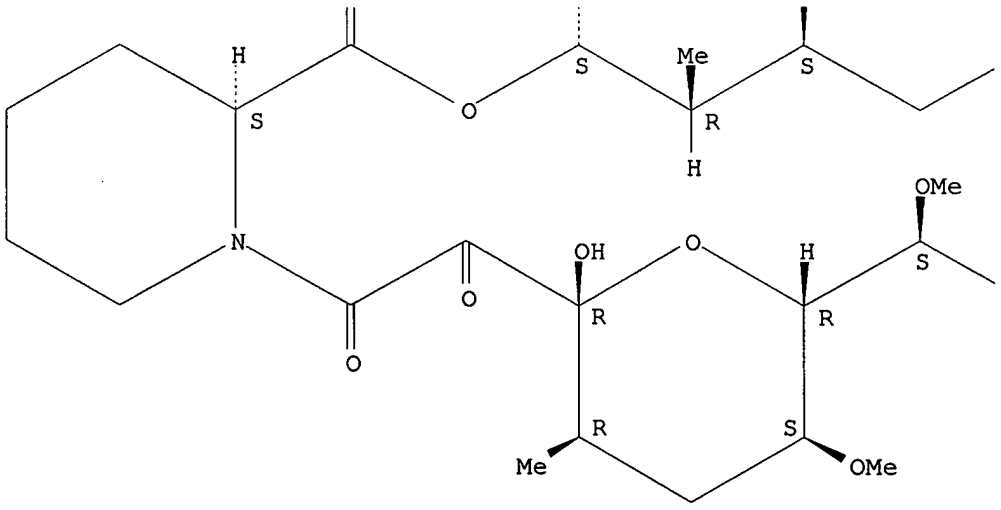
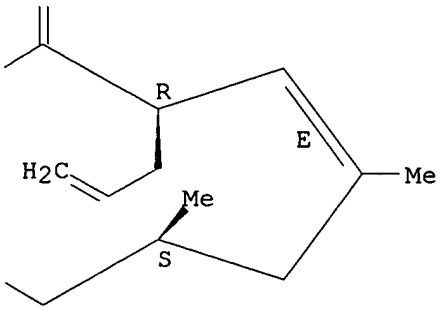
PAGE 2-A



● H_2O



9 REFERENCES IN FILE CA (1962 TO DATE)
9 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:8348

REFERENCE 2: 136:156478

REFERENCE 3: 134:46789

REFERENCE 4: 133:217476

REFERENCE 5: 131:262649

REFERENCE 6: 130:332620

REFERENCE 7: 127:185226

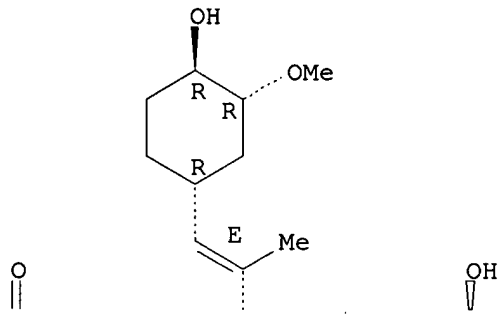
REFERENCE 8: 126:181043

REFERENCE 9: 107:175741

L13 ANSWER 11 OF 12 REGISTRY COPYRIGHT 2003 ACS
RN **104987-12-4** REGISTRY
CN 15,19-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosine-1,7,20,21(4H,23H)-tetrone, 8-ethyl-5,6,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-5,19-dihydroxy-3-[(1E)-2-[(1R,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-, (3S,4R,5S,8R,9E,12S,14S,15R,16S,18R,19R,26aS)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 15,19-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosine-1,7,20,21(4H,23H)-tetrone, 8-ethyl-5,6,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-5,19-dihydroxy-3-[2-(4-hydroxy-3-methoxycyclohexyl)-1-methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-, [3S-[3R*[E(1S*,3S*,4S*)],4S*,5R*,8S*,9E,12R*,14R*,15S*,16R*,18S*,19S*,26aR*]]-
OTHER NAMES:
CN Ascomycin
CN FK 520
CN FR 520
CN FR 900520
CN Immunomycin
CN L 683590
FS STEREOSEARCH
DR 11011-38-4, 159430-76-9, 126340-36-1, 133876-12-7, 136457-58-4, 137767-75-0, 148400-02-6
MF C43 H69 N O12

SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IFICDB, IFIUDB, MEDLINE, NAPRALERT, PHAR, PROMT, RTECS*, SYNTHLINE, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.
Double bond geometry as described by E or Z.



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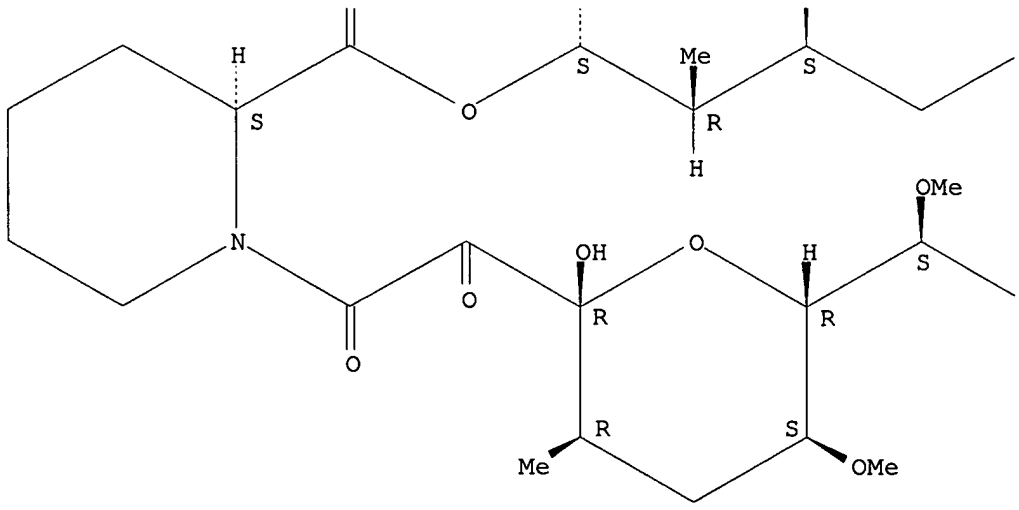
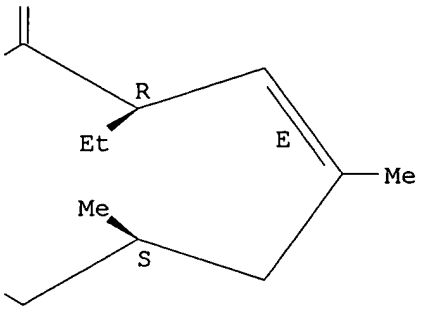




PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

240 REFERENCES IN FILE CA (1962 TO DATE)
38 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
241 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:66697

REFERENCE 2: 138:23766

REFERENCE 3: 138:8377

REFERENCE 4: 138:8348

REFERENCE 5: 137:299948

REFERENCE 6: 137:237728

REFERENCE 7: 137:218731

REFERENCE 8: 137:215879

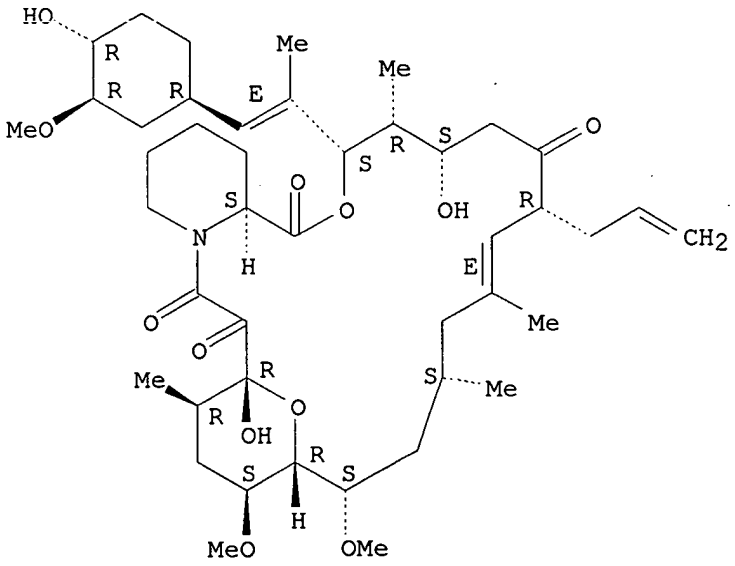
REFERENCE 9: 137:210973

REFERENCE 10: 137:185341

L13 ANSWER 12 OF 12 REGISTRY COPYRIGHT 2003 ACS
RN **104987-11-3** REGISTRY
CN 15,19-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosine-1,7,20,21(4H,23H)-tetrone, 5,6,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-5,19-dihydroxy-3-[(1E)-2-[(1R,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-8-(2-propenyl)-, (3S,4R,5S,8R,9E,12S,14S,15R,16S,18R,19R,26aS)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 15,19-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosine-1,7,20,21(4H,23H)-tetrone, 5,6,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-5,19-dihydroxy-3-[2-(4-hydroxy-3-methoxycyclohexyl)-1-methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-8-(2-propenyl)-, [3S-[3R*[E(1S*,3S*,4S*)],4S*,5R*,8S*,9E,12R*,14R*,15S*,16R*,18S*,19S*,26aR*]]-
OTHER NAMES:
CN (-)-FK 506
CN FK 506
CN FR 900506
CN Fujimycin
CN L 679934

CN Prograf
CN Protopic
CN Tacrolimus
CN Tsukubaenolide
FS STEREOSEARCH
MF C44 H69 N O12
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IFICDB, IFIUDB, MEDLINE, MRCK*, PHAR, PHARMASEARCH, PROMT, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3730 REFERENCES IN FILE CA (1962 TO DATE)
125 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3747 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:126929

REFERENCE 2: 138:117567

REFERENCE 3: 138:117411

REFERENCE 4: 138:117409

REFERENCE 5: 138:117405

REFERENCE 6: 138:112119

REFERENCE 7: 138:100720

REFERENCE 8: 138:100501

REFERENCE 9: 138:95621

REFERENCE 10: 138:95376

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

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L10        3995 SEA FILE=HCAPLUS L9
L11         101 SEA FILE=HCAPLUS L10 AND (EYE? OR OPHTHAL? OR OCUL?)
L12          27 SEA FILE=HCAPLUS L10 (L) (EYE? OR OPHTHAL? OR OCUL?)
L14           7 SEA FILE=HCAPLUS L11 AND DRY
L15           3 SEA FILE=HCAPLUS L14 NOT L12
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L15 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:696457 HCAPLUS
DOCUMENT NUMBER: 137:237728
TITLE: Peptide conjugates for enhancing drug delivery across and into epithelial tissues
INVENTOR(S): Rothbard, Jonathan B.; Wender, Paul A.; McGrane, P. Leo; Sista, Lalitha V. S.; Kirschberg, Thorsten A.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 80 pp., Cont.-in-part of U.S. Ser. No. 648,400.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002127198	A1	20020912	US 2001-792480	20010223
WO 2002067917	A1	20020906	WO 2002-US5804	20020225

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WO 2002069930	A1	20020912	WO 2002-US5829	20020225

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US 2003022831 A1 20030130 US 2002-83960 20020225
PRIORITY APPLN. INFO.: US 1999-150510P P 19990824
US 2000-648400 A2 20000824
US 2001-792480 A 20010223
OTHER SOURCE(S): MARPAT 137:237728
AB This invention provides compns. and methods for enhancing delivery of drugs and other agents across epithelial tissues, including the skin, gastrointestinal tract, pulmonary epithelium, **ocular** tissues and the like. The compns. and methods are also useful for delivery across endothelial tissues, including the blood brain barrier. The compns. and methods employ a delivery enhancing transporter that has sufficient guanidino or amidino side-chain moieties to enhance delivery of a compd. conjugated to the reagent across one or more layers of the tissue, compared to the non-conjugated compd. The delivery-enhancing polymers include, for example, poly-arginine mols. that are preferably between about 6 and 25 residues in length. E.g., biotinylated polymers of D-arginine were prepd. and their penetration into the skin of nude mice studied.
IT **104987-11-3,** FK 506
RL: RCT (Reactant); RACT (Reactant or reagent)
(peptide conjugates for enhancing drug delivery across and into epithelial tissues)
IT **455282-21-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(peptide conjugates for enhancing drug delivery across and into epithelial tissues)
IT **455282-16-3P 455282-17-4P 455282-18-5P 455282-19-6P 455282-20-9P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(peptide conjugates for enhancing drug delivery across and into epithelial tissues)
IT **104987-12-4,** Ascomycin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptide conjugates for enhancing drug delivery across and into epithelial tissues)

L15 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:539697 HCAPLUS
DOCUMENT NUMBER: 137:94011
TITLE: Preparation of peptide compounds having NOS inhibiting activity
INVENTOR(S): Shima, Ichiro; Ohkawa, Takehiko; Sato, Kentaro; Ishibashi, Naoki; Imamura, Kenichiro
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002055541	A2	20020718	WO 2001-JP11067	20011218

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UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: AU 2001-2371 A 20010102
AU 2001-7506 A 20010905

OTHER SOURCE(S): MARPAT 137:94011

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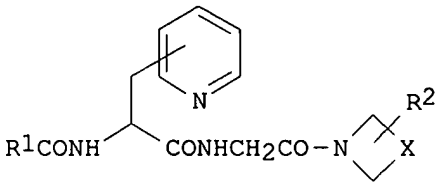

I

AB Peptides I (R1 = halobenzofuranyl or halostyryl; R2 = substituted hydroxy, mercapto, or sulfonyl; X = CH2, CH2CH2, CH2CH2CH2) or their pharmaceutically acceptable salts were prepd. for the prevention and/or treatment of nitric oxide-mediated diseases. Thus, 5-chloro-N-[(1S)-2-oxo-2-[[2-oxo-2-[4-(1,3-thiazol-2-yloxy)-1-piperidinyl]ethyl]amino]-1-(2-pyridylmethyl)ethyl]-1-benzofuran-2-carboxamide (II) was prepd. via amidation reaction and showed 100% inhibition of nitric acid. The combination of compds. I and FK507 dramatically prolonged graft survival in rat cardiac allograft.

IT **104987-11-3**, Fk506
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of peptide compds. having NOS inhibiting activity)

L15 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:338558 HCAPLUS
DOCUMENT NUMBER: 134:340709
TITLE: Preparation of substituted dipeptides having NOS inhibiting activity
INVENTOR(S): Shima, Ichiro; Ohkawa, Takehiko; Ohne, Kazuhiko; Sato, Kentaro; Ishibashi, Naoki; Imamura, Kenichiro
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032690	A1	20010510	WO 2000-JP7579	20001027
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RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1226159	A1	20020731	EP 2000-970164	20001027
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				

PRIORITY APPLN. INFO.: AU 1999-3868 A 19991104
WO 2000-JP7579 W 20001027

OTHER SOURCE(S): MARPAT 134:340709

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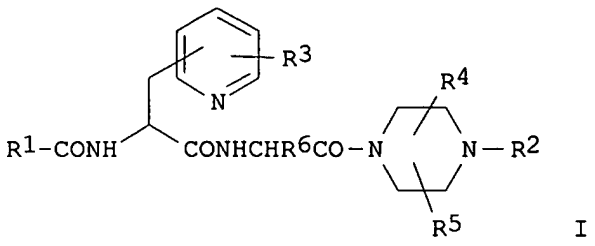

I

AB Dipeptides I [R1 is benzofuranyl or styryl substituted by halogen; R2 is (un)substituted Ph, pyridyl, thienyl, or thiazolyl; R3, R6 = H or lower alkoxy; R4, R5 = H, lower alkyl or optionally protected hydroxy(lower)alkyl] or their pharmaceutically acceptable salts were prepd. for use in the prevention and/or treatment of nitric oxide-mediated diseases. Thus, 5-chloro-N-[(1S)-2-[[2-[4-(4-chlorophenyl)-1-piperazinyl]-2-oxoethyl]amino]-2-oxo-1-(2-pyridylmethyl)ethyl]-1-benzofuran-2-carboxamide (II) was prepd. via amidation reaction and showed 100% inhibition of nitric acid. The combination of compd. II and FK507 dramatically prolonged graft survival in rat cardiac allograft.

IT **104987-11-3**, Fk506
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of substituted dipeptides having NOS inhibiting activity)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> select hit rn l15 1-3
E13 THROUGH E20 ASSIGNED

=> fil reg
FILE 'REGISTRY' ENTERED AT 12:08:15 ON 26 FEB 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 25 FEB 2003 HIGHEST RN 494824-56-5
DICTIONARY FILE UPDATES: 25 FEB 2003 HIGHEST RN 494824-56-5

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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(104987-11-3/RN)

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               455282-21-0/BI)

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L16  ANSWER 1 OF 8  REGISTRY  COPYRIGHT 2003 ACS
RN   455282-21-0  REGISTRY
CN   1H-Pyrrole-1-hexanoic acid, 2,5-dihydro-2,5-dioxo-,
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     1,3,4,5,6,8,11,12,13,14,15,16,17,18,19,20,21,23,24,25,26,26a-docosahydro-
     5,19-dihydroxy-3-[(1E)-2-[(1R,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-
     methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-1,20,21-trioxo-8-(2-
     propenyl)-15,19-epoxy-7H-pyrido[2,1-c][1,4]oxaazacyclotricosin-7-
     ylidene]hydrazide (9CI)  (CA INDEX NAME)
FS   STEREOSEARCH
MF   C54 H82 N4 O14
SR   CA
LC   STN Files:   CA, CAPLUS, USPATFULL

Absolute stereochemistry.
Double bond geometry as described by E or Z.
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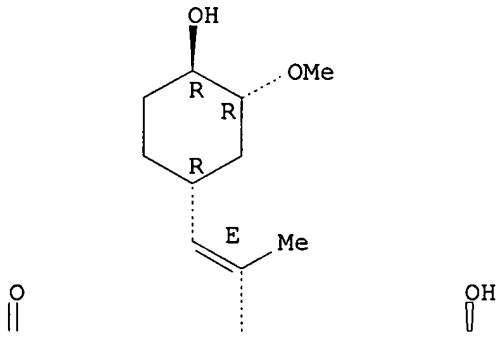

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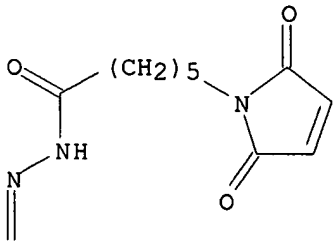

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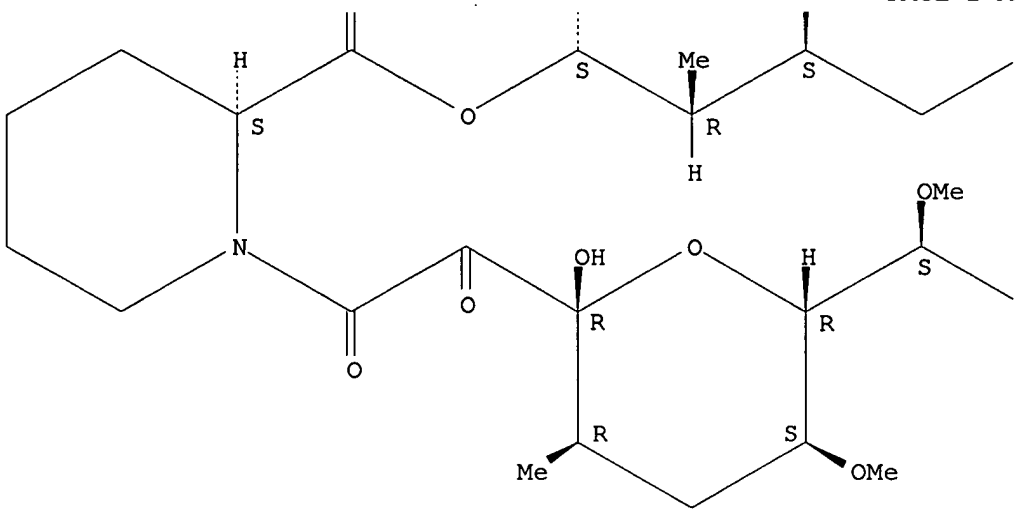

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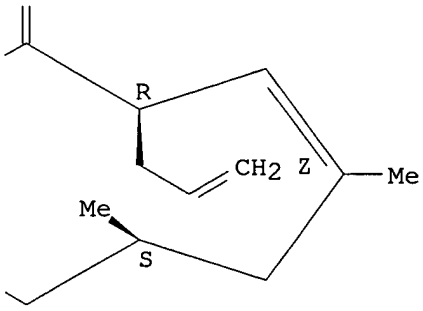

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:237728

REFERENCE 2: 137:222033

L16 ANSWER 2 OF 8 REGISTRY COPYRIGHT 2003 ACS
RN **455282-20-9** REGISTRY
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FS PROTEIN SEQUENCE; STEREOSEARCH
MF C99 H174 N34 O22 S
SR CA

LC STN Files: CA, CAPLUS, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.
Double bond geometry as described by E or Z.

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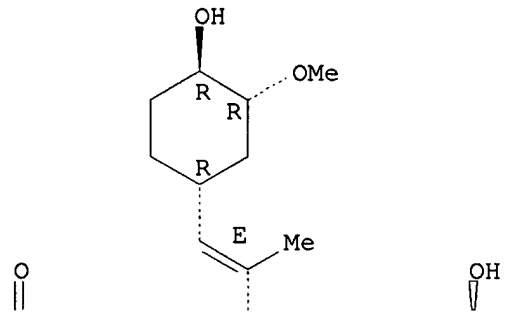

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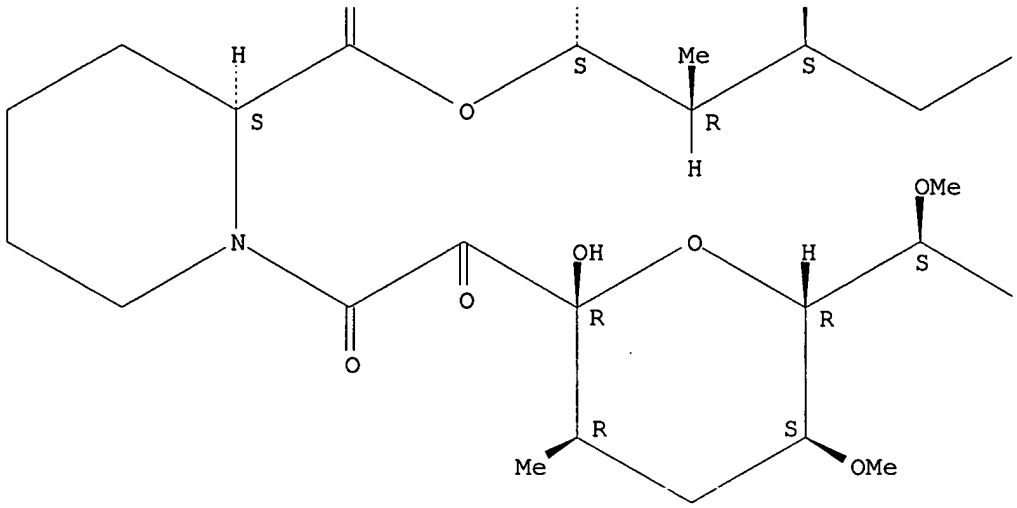

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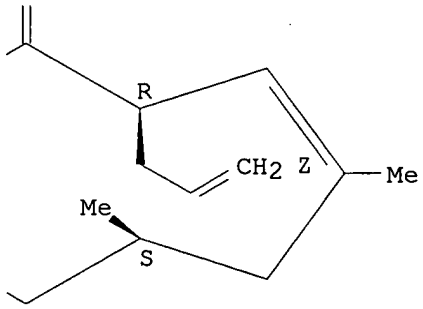

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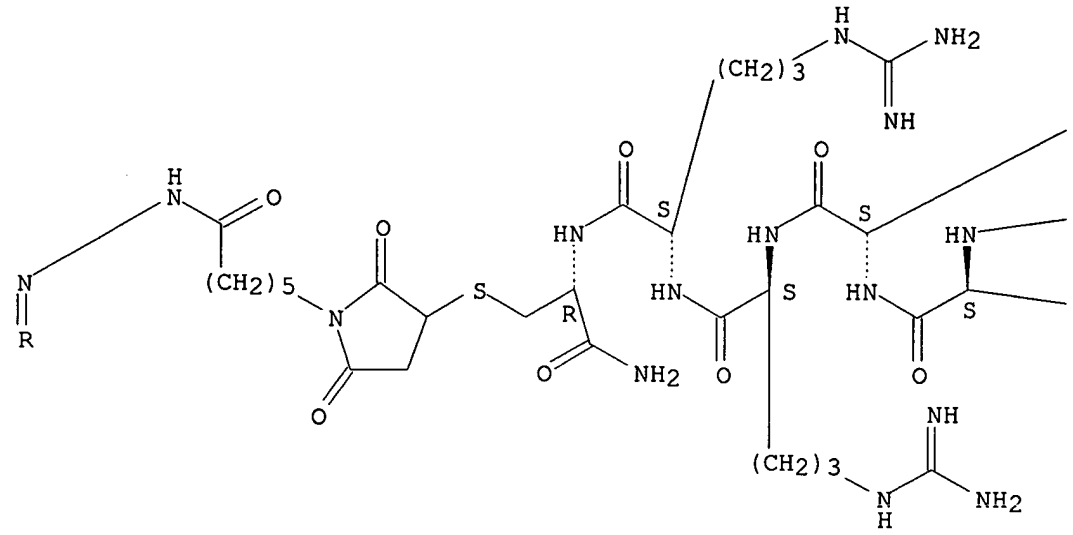

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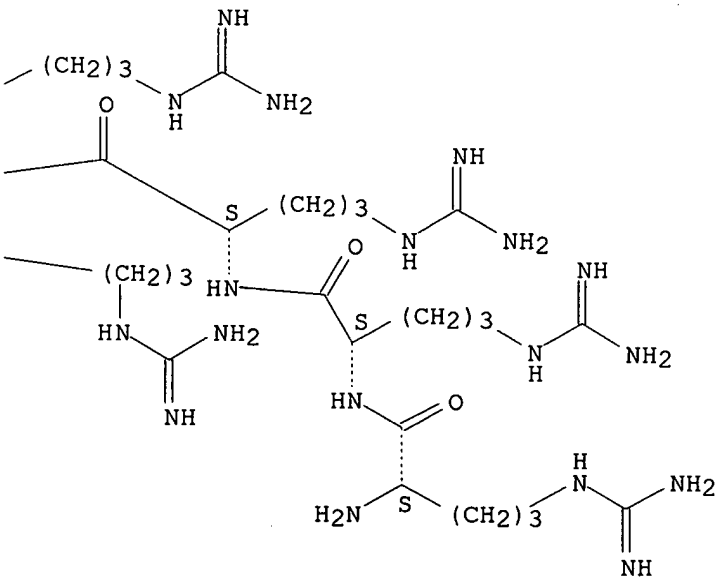

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:237728

REFERENCE 2: 137:222033

L16 ANSWER 3 OF 8 REGISTRY COPYRIGHT 2003 ACS

RN **455282-19-6** REGISTRY
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FS PROTEIN SEQUENCE; STEREOSEARCH
MF C99 H174 N34 O22 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

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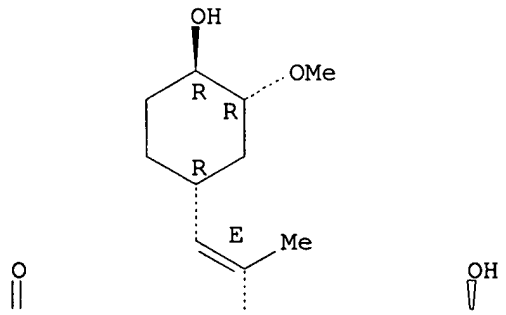
Double bond geometry as described by E or Z.



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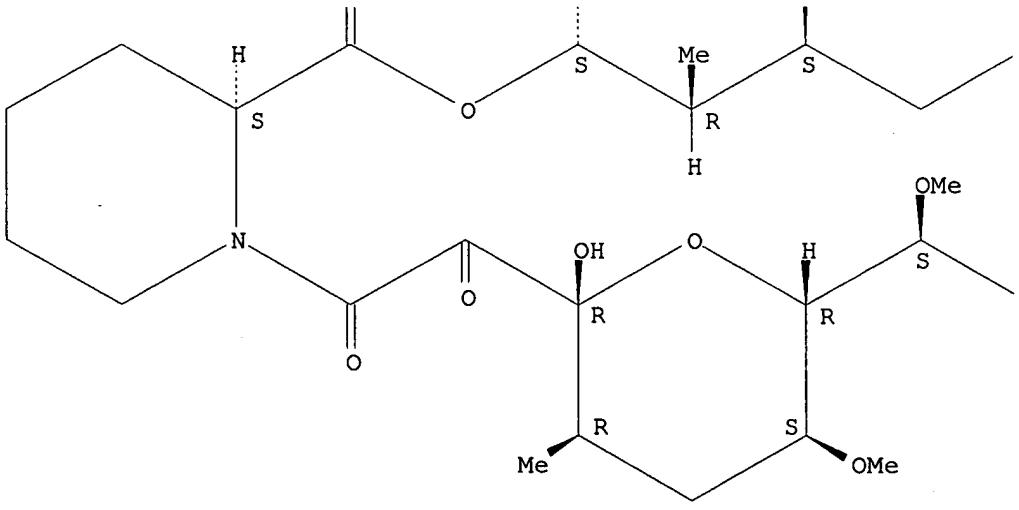

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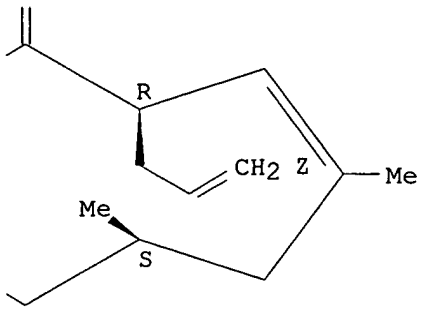

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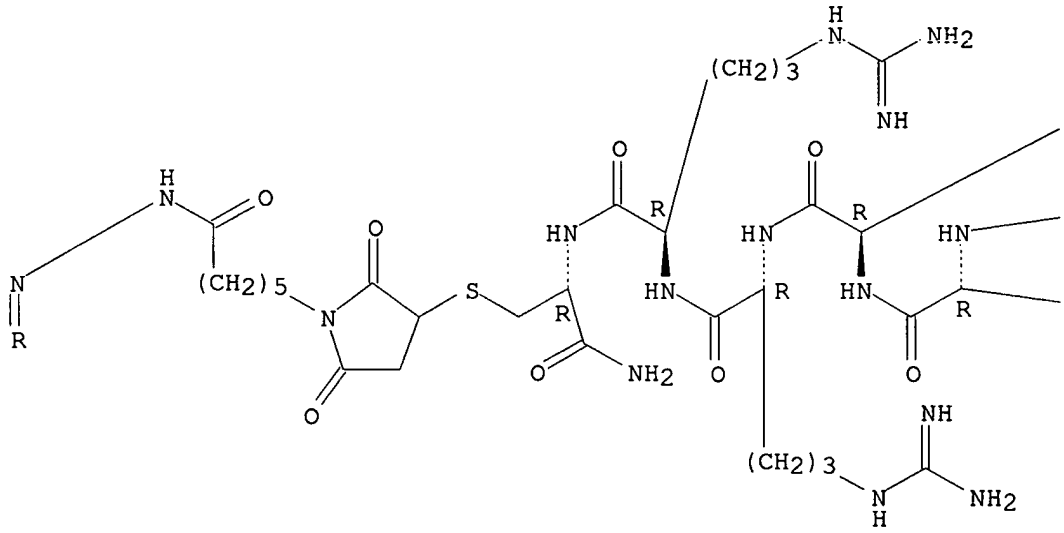

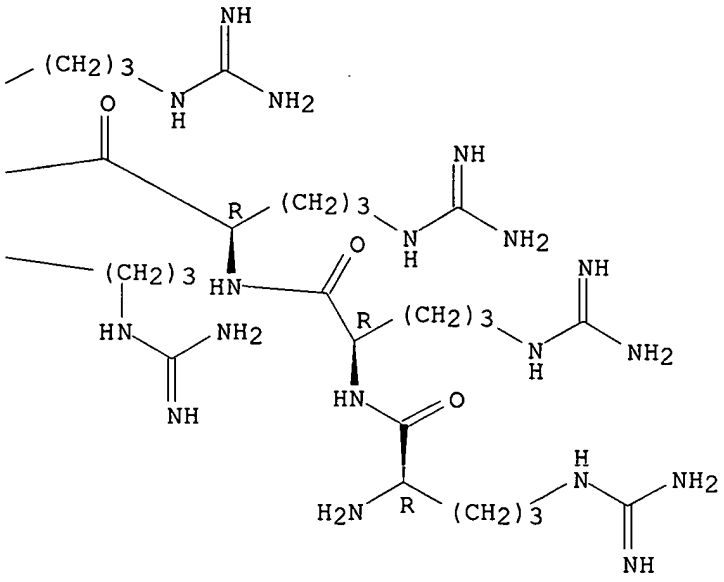

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2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

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REFERENCE 2: 137:222033

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FS STEREOSEARCH
MF C73 H115 N9 O18 S2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.
Double bond geometry as described by E or Z.

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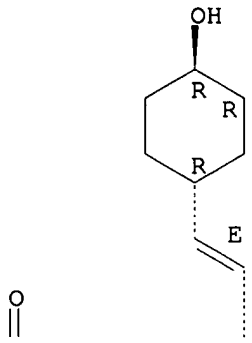

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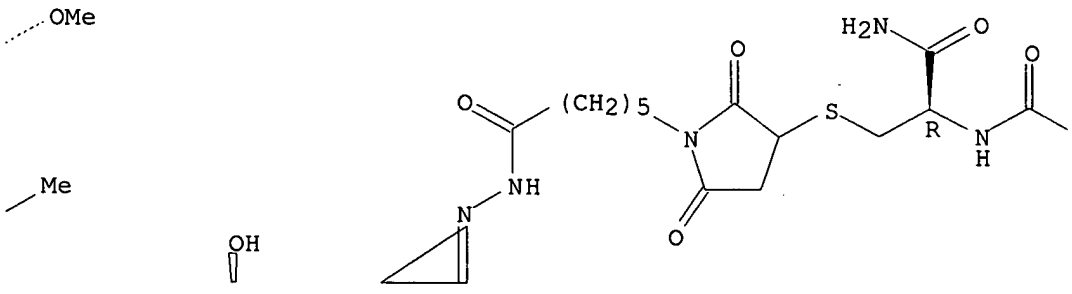

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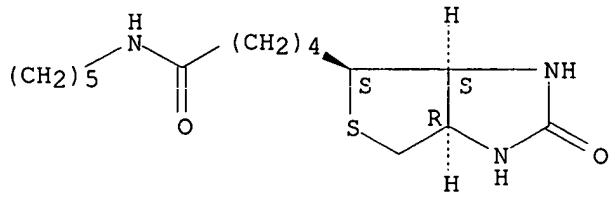

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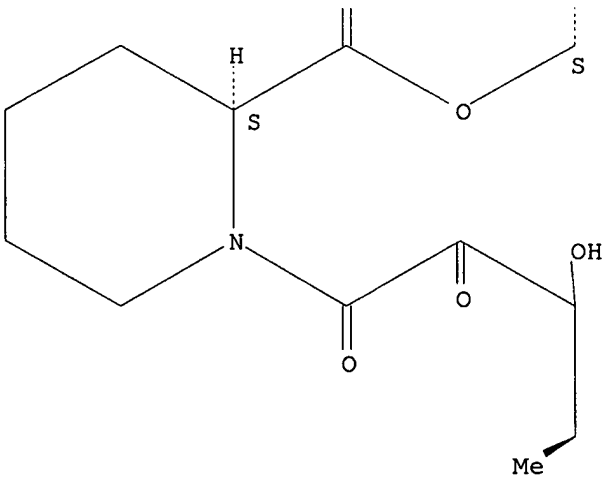
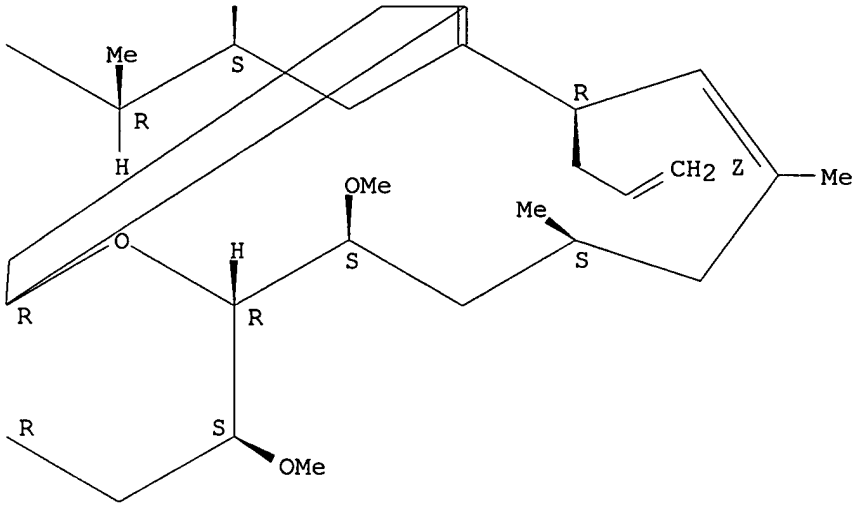




PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:237728

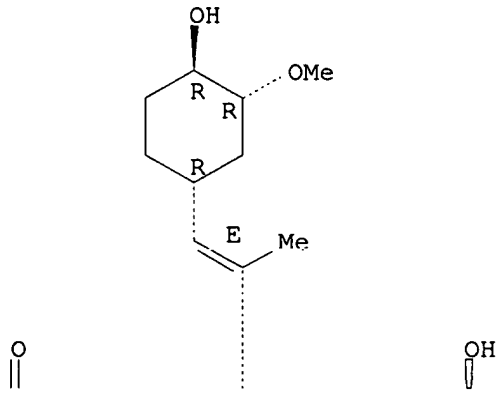
REFERENCE 2: 137:222033

L16 ANSWER 5 OF 8 REGISTRY COPYRIGHT 2003 ACS
RN **455282-17-4** REGISTRY
CN L-Cysteinamide, N2-[6-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]amino]-1-oxohexyl]-D-arginyl-D-arginyl-D-arginyl-D-arginyl-D-arginyl-D-arginyl-D-arginyl-S-[1-[6-[[(3S,4R,5S,8R,9Z,12S,14S,15R,16S,18R,19R,26aS)-1,3,4,5,6,8,11,12,13,14,15,16,17,18,19,20,21,23,24,25,26,26a-docosahydro-5,19-dihydroxy-3-[(1E)-2-[(1R,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-1,20,21-trioxo-8-(2-propenyl)-15,19-epoxy-7H-pyrido[2,1-c][1,4]oxaazacyclotricosin-7-ylidene]hydrazino]-6-oxohexyl]-2,5-dioxo-3-pyrrolidinyl]- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C115 H199 N37 O25 S2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.
Double bond geometry as described by E or Z.

PAGE 1-A



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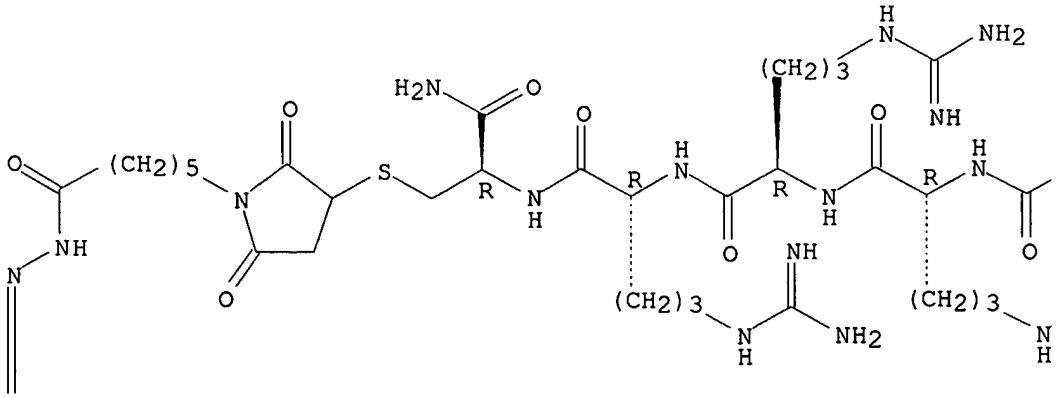

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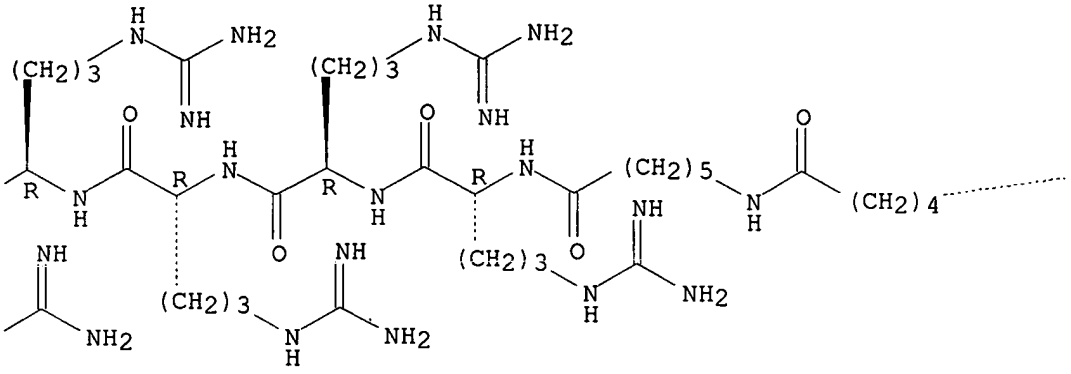

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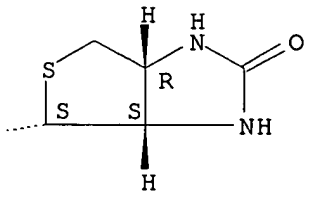

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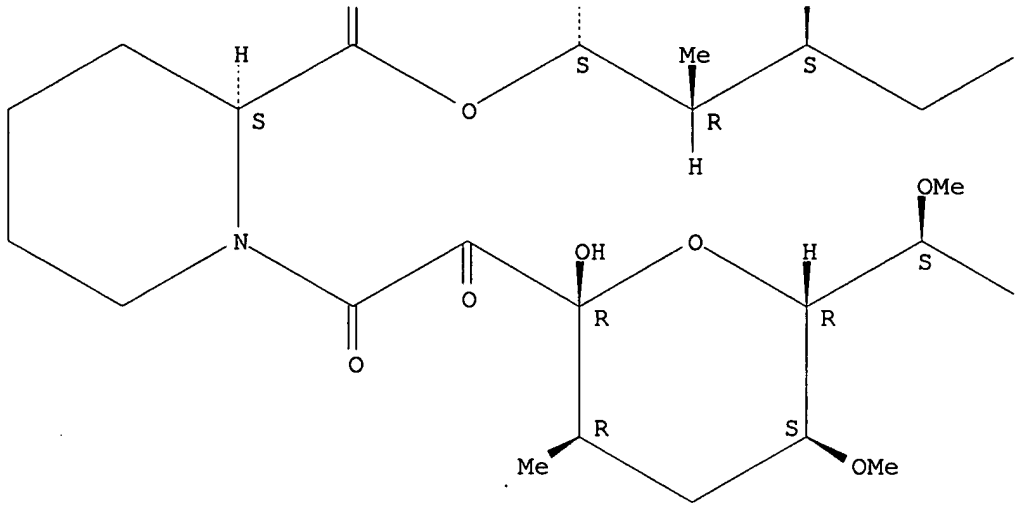

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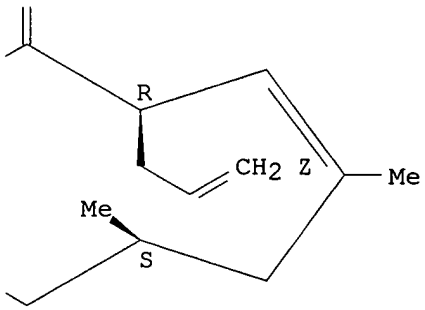


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:237728

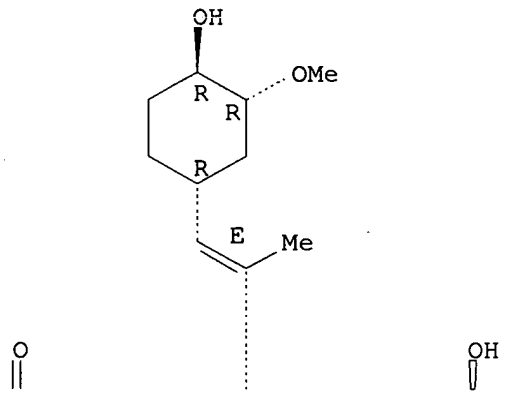
REFERENCE 2: 137:222033

L16 ANSWER 6 OF 8 REGISTRY COPYRIGHT 2003 ACS
RN **455282-16-3** REGISTRY
CN L-Cysteinamide, N2-[6-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]amino]-1-oxohexyl]-D-arginyl-D-arginyl-D-arginyl-D-arginyl-D-arginyl-D-arginyl-D-arginyl-D-arginyl-S-[1-[6-[[(3S,4R,5S,8R,9Z,12S,14S,15R,16S,18R,19R,26aS)-1,3,4,5,6,8,11,12,13,14,15,16,17,18,19,20,21,23,24,25,26,26a-docosahydro-5,19-dihydroxy-3-[(1E)-2-[(1R,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-1,20,21-trioxo-8-(2-propenyl)-15,19-epoxy-7H-pyrido[2,1-c][1,4]oxaazacyclotricosin-7-ylidene]hydrazino]-6-oxohexyl]-2,5-dioxo-3-pyrrolidinyl]- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH

MF C127 H223 N45 O27 S2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.
Double bond geometry as described by E or Z.



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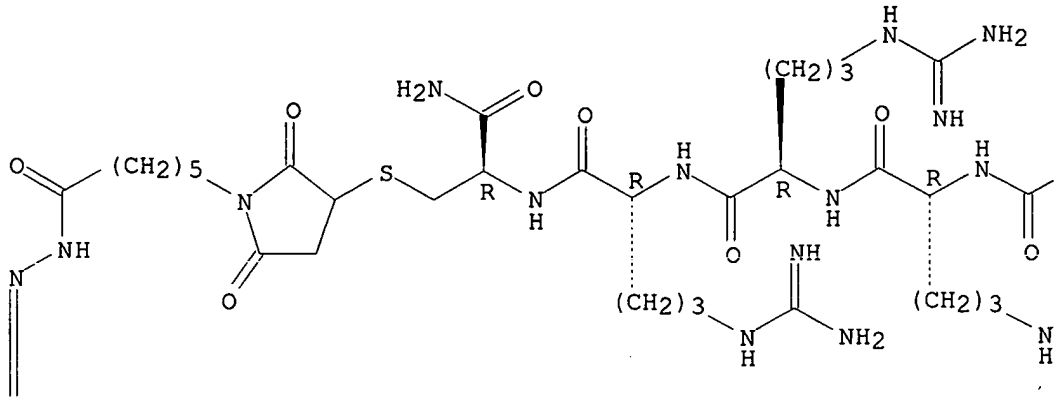

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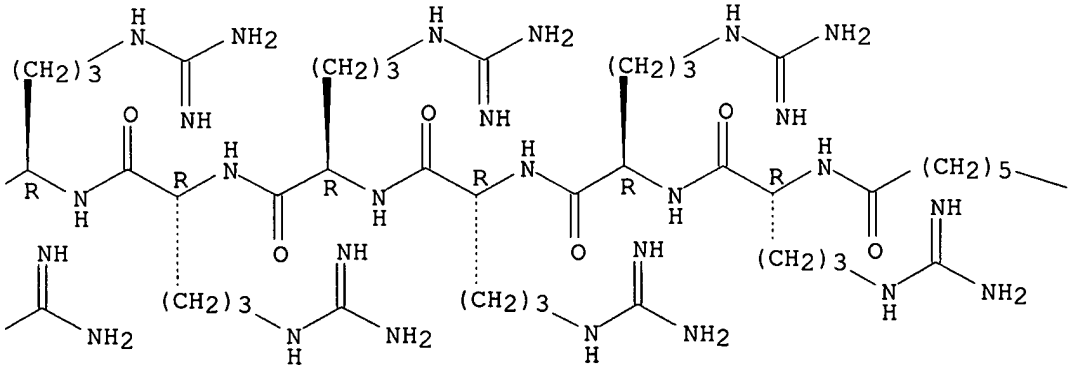

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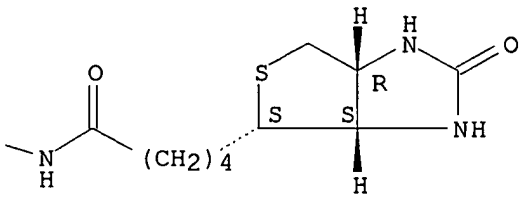

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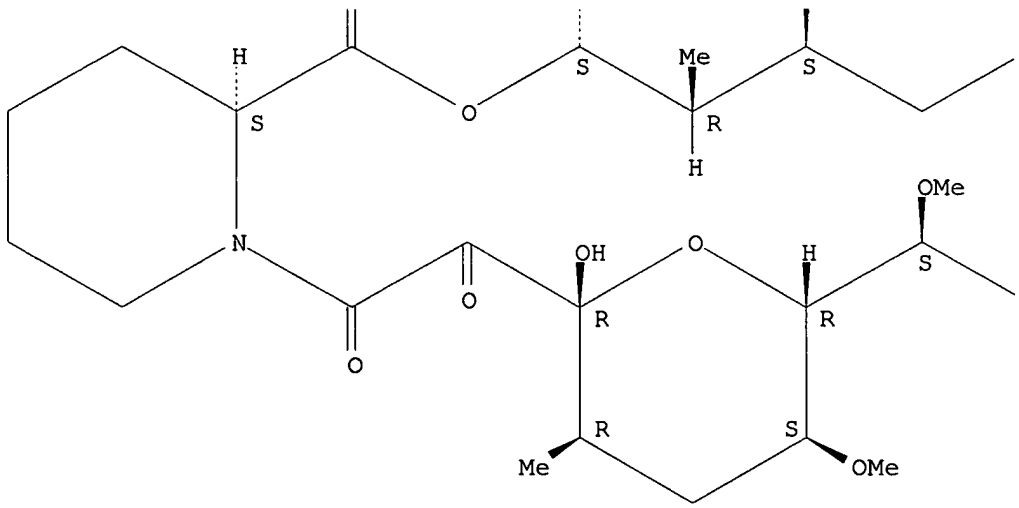

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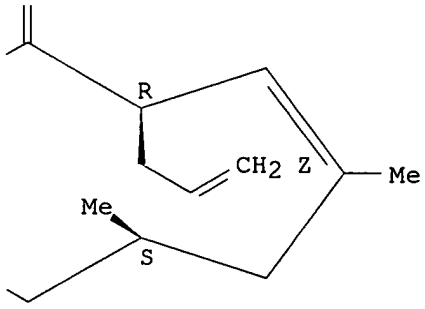

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:237728

REFERENCE 2: 137:222033

L16 ANSWER 7 OF 8 REGISTRY COPYRIGHT 2003 ACS
RN **104987-12-4** REGISTRY
CN 15,19-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosine-1,7,20,21(4H,23H)-tetrone, 8-ethyl-5,6,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-5,19-dihydroxy-3-[(1E)-2-[(1R,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-, (3S,4R,5S,8R,9E,12S,14S,15R,16S,18R,19R,26aS)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 15,19-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosine-1,7,20,21(4H,23H)-tetrone, 8-ethyl-5,6,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-5,19-dihydroxy-3-[2-(4-hydroxy-3-methoxycyclohexyl)-1-methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-, [3S-[3R*[E(1S*,3S*,4S*)],4S*,5R*,8S*,9E,12R*,14R*,15S*,16R*,18S*,19S*,26aR*]]-
OTHER NAMES:
CN Ascomycin
CN FK 520
CN FR 520
CN FR 900520
CN Immunomycin
CN L 683590
FS STEREOSEARCH
DR 11011-38-4, 159430-76-9, 126340-36-1, 133876-12-7, 136457-58-4, 137767-75-0, 148400-02-6
MF C43 H69 N O12
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IFICDB, IFIUDB, MEDLINE, NAPRALERT, PHAR, PROMT, RTECS*, SYNTHLINE, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

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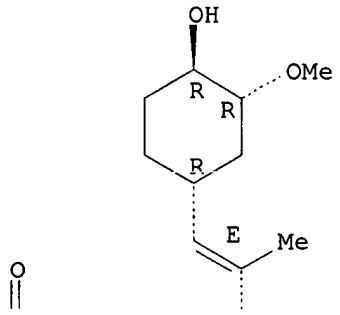

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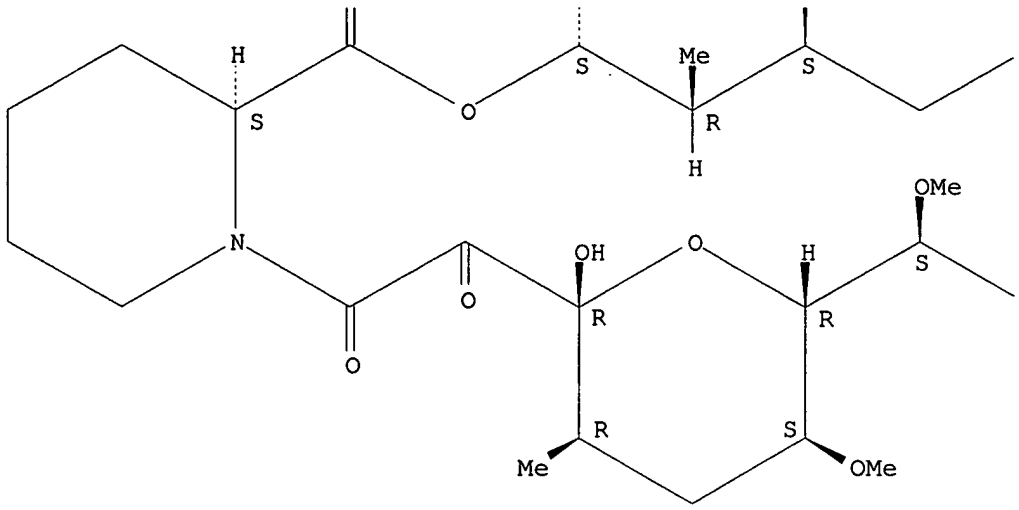

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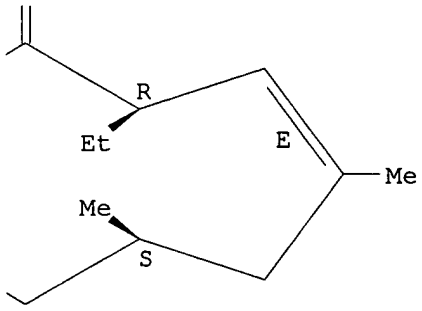


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

240 REFERENCES IN FILE CA (1962 TO DATE)
38 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
241 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:66697

REFERENCE 2: 138:23766

REFERENCE 3: 138:8377

REFERENCE 4: 138:8348

REFERENCE 5: 137:299948

REFERENCE 6: 137:237728

REFERENCE 7: 137:218731

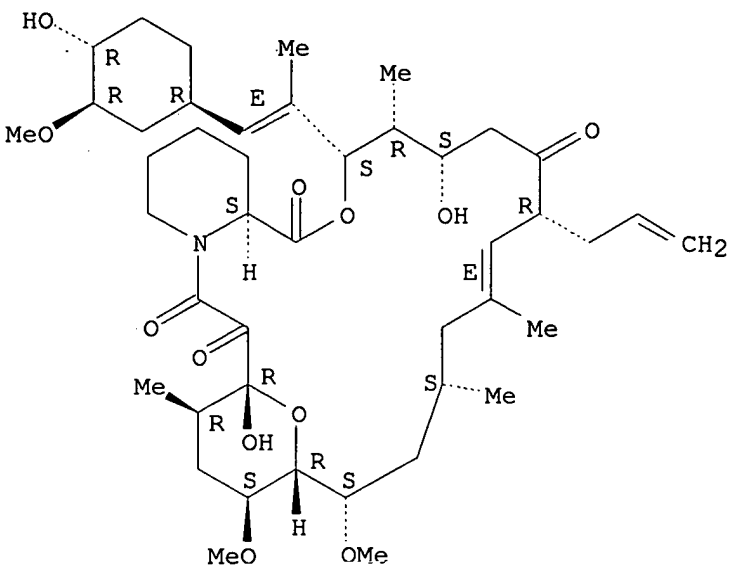
REFERENCE 8: 137:215879

REFERENCE 9: 137:210973

REFERENCE 10: 137:185341

L16 ANSWER 8 OF 8 REGISTRY COPYRIGHT 2003 ACS
RN **104987-11-3** REGISTRY
CN 15,19-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosine-1,7,20,21(4H,23H)-tetrone, 5,6,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-5,19-dihydroxy-3-[(1E)-2-[(1R,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-8-(2-propenyl)-, (3S,4R,5S,8R,9E,12S,14S,15R,16S,18R,19R,26aS)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 15,19-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosine-1,7,20,21(4H,23H)-tetrone, 5,6,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-5,19-dihydroxy-3-[2-(4-hydroxy-3-methoxycyclohexyl)-1-methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-8-(2-propenyl)-, [3S-[3R*[E(1S*,3S*,4S*)],4S*,5R*,8S*,9E,12R*,14R*,15S*,16R*,18S*,19S*,26aR*]]-
OTHER NAMES:
CN (-)-FK 506
CN FK 506
CN FR 900506
CN Fujimycin
CN L 679934
CN Prograf
CN Protopic
CN Tacrolimus
CN Tsukubaenolide
FS STEREOSEARCH
MF C44 H69 N O12
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IFICDB, IFIUDB, MEDLINE, MRCK*, PHAR, PHARMASEARCH, PROMT, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3730 REFERENCES IN FILE CA (1962 TO DATE)
125 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3747 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:126929

REFERENCE 2: 138:117567

REFERENCE 3: 138:117411

REFERENCE 4: 138:117409

REFERENCE 5: 138:117405

REFERENCE 6: 138:112119

REFERENCE 7: 138:100720

REFERENCE 8: 138:100501

REFERENCE 9: 138:95621

REFERENCE 10: 138:95376